

## Description

# BIOINFORMATICALLY DETECTABLE GROUP OF NOVEL VIRAL REGULATORY GENES AND USES THEREOF

### BACKGROUND OF INVENTION

### FIELD OF THE INVENTION

[0001] The present invention relates to a group of bioinformatically detectable novel viral RNA regulatory genes, here identified as "viral genomic address messenger" or "VGAM" genes.

### DESCRIPTION OF PRIOR ART

[0002] Small RNAs are known to perform diverse cellular functions, including post-transcriptional gene expression regulation. The first two such RNA genes, Lin-4 and Let-7, were identified by genetic analysis of *Caenorhabditis Elegans* (*Elegans*) developmental timing, and were termed short temporal RNA (stRNA) (Wightman, B., Ha, I., Ruvkun, G., *Cell* 75, 855 (1993); Erdmann, V.A. et al., *Nucleic*



Acids Res. 29, 189 (2001); Lee, R. C., Feinbaum, R. L., Ambros, V., Cell 75, 843 (1993); Reinhart, B. et al., Nature 403, 901 (2000)).

[0003] Lin-4 and Let-7 each transcribe a ~22 nucleotide (nt) RNA, which acts a post transcriptional repressor of target mRNAs, by binding to elements in the 3'-untranslated region (UTR) of these target mRNAs, which are complimentary to the 22 nt sequence of Lin-4 and Let-7 respectively. While Lin-4 and Let-7 are expressed at different developmental stage, first larval stage and fourth larval stage respectively, both specify the temporal progression of cell fates, by triggering post-transcriptional control over other genes (Wightman, B., Ha, I., Ruvkun, G., Cell 75, 855 (1993); Slack et al., Mol.Cell 5 ,659 (2000)). Let-7 as well as its temporal regulation have been demonstrated to be conserved in all major groups of bilaterally symmetrical animals, from nematodes, through flies to humans (Pasquinelli, A., et al. Nature 408 ,86 (2000)).

[0004] The initial transcription product of Lin-4 and Let-7 is a ~60-80nt RNA, the nucleotide sequence of the first half of which is partially complimentary to that of its second half, therefore allowing this RNA to fold onto itself, forming a "hairpin structure". The final gene product is a ~22nt RNA,

which is "diced" from the above mentioned "hairpin structure", by an enzyme called Dicer, which also apparently also mediates the complimentary binding of this ~22nt segment to a binding site in the 3' UTR of its target gene.

[0005] Recent studies have uncovered 93 new genes in this class, now referred to as micro RNA or miRNA genes, in genomes of *Elegans*, *Drosophila*, and Human (Lagos-Quintana, M., Rauhut, R., Lendeckel, W., Tuschl, T., *Science* 294 ,853 (2001); Lau, N.C., Lim, L.P., Weinstein, E.G., Bartel, D.P., *Science* 294 ,858 (2001); Lee, R.C., Ambros, V., *Science* 294 ,862 (2001). Like the well studied Lin-4 and Let-7, all newly found MIR genes produce a ~60–80nt RNA having a nucleotide sequence capable of forming a "hairpin structure". Expressions of the precursor ~60–80nt RNA and of the resulting diced ~22nt RNA of most of these newly discovered MIR genes have been detected.

[0006] Based on the striking homology of the newly discovered MIR genes to their well-studied predecessors Lin-4 and Let-7, the new MIR genes are believed to have a similar basic function as that of Lin-4 and Let-7: modulation of target genes by complimentary binding to the UTR of these target genes, with special emphasis on modulation

of developmental control processes. This is despite the fact that the above mentioned recent studies did not find target genes to which the newly discovered MIR genes complementarily bind. While existing evidence suggests that the number of regulatory RNA genes "may turn out to be very large, numbering in the hundreds or even thousands in each genome", detecting such genes is challenging (Ruvkun G., "Perspective: Glimpses of a tiny RNA world", Science 294 ,779 (2001)).

[0007] The ability to detect novel RNA genes is limited by the methodologies used to detect such genes. All RNA genes identified so far either present a visibly discernable whole body phenotype, as do Lin-4 and Let-7 (Wightman et. al., Cell 75, 855 (1993); Reinhart et al., Nature 403, 901 (2000)), or produce significant enough quantities of RNA so as to be detected by the standard biochemical genomic techniques, as do the 93 recently detected miRNA genes. Since a limited number clones were sequenced by the researchers discovering these genes, 300 by Bartel and 100 by Tuschl (Bartel et. al., Science 294 ,858 (2001); Tuschl et. al., Science 294 ,853 (2001)), the RNA genes found can not be much rarer than 1% of all RNA genes. The recently detected miRNA genes therefore represent the more

prevalent among the miRNA gene family.

[0008] Current methodology has therefore been unable to detect RNA genes which either do not present a visually discernable whole body phenotype, or are rare (e.g. rarer than 0.1% of all RNA genes), and therefore do not produce significant enough quantities of RNA so as to be detected by standard biochemical technique. To date, miRNA have not been detected in viruses.

#### **SUMMARY OF INVENTION**

[0009] The present invention relates to a novel group of bioinformatically detectable, viral regulatory RNA genes, which repress expression of host target host genes, by means of complementary hybridization to binding sites in untranslated regions of these host target host genes. It is believed that this novel group of viral genes represent a pervasive viral mechanism of attacking hosts, and that therefore knowledge of this novel group of viral genes may be useful in preventing and treating viral diseases.

[0010] In various preferred embodiments, the present invention seeks to provide improved method and system for detection and prevention of viral disease, which is mediated by this group of novel viral genes.

[0011] Accordingly, the invention provides several substantially

pure nucleic acids (e.g., genomic nucleic acid, cDNA or synthetic nucleic acid) each encoding a novel viral gene of the VGAM group of gene, vectors comprising the nucleic acids , probes comprising the nucleic acids , a method and system for selectively modulating translation of known "target" genes utilizing the vectors, and a method and system for detecting expression of known "target" genes utilizing the probe.

[0012] By "substantially pure nucleic acid" is meant nucleic acid that is free of the genes which, in the naturally-occurring genome of the organism from which the nucleic acid of the invention is derived, flank the genes discovered and isolated by the present invention. The term therefore includes, for example, a recombinant nucleic acid which is incorporated into a vector, into an autonomously replicating plasmid or virus, or into the genomic nucleic acid of a prokaryote or eukaryote at a site other than its natural site; or which exists as a separate molecule (e.g., a cDNA or a genomic or cDNA fragment produced by PCR or restriction endonuclease digestion) independent of other sequences. It also includes a recombinant nucleic acid which is part of a hybrid gene encoding additional polypeptide sequence.

[0013] "Inhibiting translation" is defined as the ability to prevent synthesis of a specific protein encoded by a respective gene, by means of inhibiting the translation of the mRNA of this gene. "Translation inhibitor site" is defined as the minimal nucleic acid sequence sufficient to inhibit translation.

[0014] There is thus provided in accordance with a preferred embodiment of the present invention a bioinformatically detectable novel viral gene encoding substantially pure nucleic acid wherein: RNA encoded by the bioinformatically detectable novel viral gene is about 18 to about 24 nucleotides in length, and originates from an RNA precursor, which RNA precursor is about 50 to about 120 nucleotides in length, a nucleotide sequence of a first half of the RNA precursor is a partial inversed-reversed sequence of a nucleotide sequence of a second half thereof, a nucleotide sequence of the RNA encoded by the novel viral gene is a partial inversed-reversed sequence of a nucleotide sequence of a binding site associated with at least one host target gene, and a function of the novel viral gene is bioinformatically deducible.

[0015] There is further provided in accordance with another preferred embodiment of the present invention a method for

anti-viral treatment comprising neutralizing said RNA.

[0016] Further in accordance with a preferred embodiment of the present invention the neutralizing comprises: synthesizing a complementary nucleic acid molecule, a nucleic sequence of which complementary nucleic acid molecule is a partial inversed-reversed sequence of said RNA, and transfecting host cells with the complementary nucleic acid molecule, thereby complementarily binding said RNA.

[0017] Further in accordance with a preferred embodiment of the present invention the neutralizing comprises immunologically neutralizing.

[0018] There is still further provided in accordance with another preferred embodiment of the present invention a bioinformatically detectable novel viral gene encoding substantially pure nucleic acid wherein: RNA encoded by the bioinformatically detectable novel viral gene includes a plurality of RNA sections, each of the RNA sections being about 50 to about 120 nucleotides in length, and including an RNA segment, which RNA segment is about 18 to about 24 nucleotides in length, a nucleotide sequence of a first half of each of the RNA sections encoded by the novel viral gene is a partial inversed-reversed sequence of nucleotide sequence of a second half thereof, a nucleotide

sequence of each of the RNA segments encoded by the novel viral gene is a partial inversed–reversed sequence of the nucleotide sequence of a binding site associated with at least one target host gene, and a function of the novel viral gene is bioinformatically deducible from the following data elements: the nucleotide sequence of the RNA encoded by the novel viral gene, a nucleotide sequence of the at least one target host gene, and function of the at least one target host gene.

[0019] Further in accordance with a preferred embodiment of the present invention the function of the novel viral gene is bioinformatically deducible from the following data elements: the nucleotide sequence of the RNA encoded by the bioinformatically detectable novel viral gene, a nucleotide sequence of the at least one target host gene, and a function of the at least one target host gene.

[0020] Still further in accordance with a preferred embodiment of the present invention the RNA encoded by the novel viral gene complementarily binds the binding site associated with the at least one target host gene, thereby modulating expression of the at least one target host gene.

[0021] Additionally in accordance with a preferred embodiment of the present invention the binding site associated with



at least one target host gene is located in an untranslated region of RNA encoded by the at least one target host gene.

[0022] Moreover in accordance with a preferred embodiment of the present invention the function of the novel viral gene is selective inhibition of translation of the at least one target host gene, which selective inhibition includes complementary hybridization of the RNA encoded by the novel viral gene to the binding site.

[0023] Further in accordance with a preferred embodiment of the present invention the invention includes a vector including the DNA.

[0024] Still further in accordance with a preferred embodiment of the present invention the invention includes a method of selectively inhibiting translation of at least one gene, including introducing the vector.

[0025] Moreover in accordance with a preferred embodiment of the present invention the introducing includes utilizing RNAi pathway.

[0026] Additionally in accordance with a preferred embodiment of the present invention the invention includes a gene expression inhibition system including: the vector, and a vector inserter, functional to insert the vector into a cell,

thereby selectively inhibiting translation of at least one gene.

[0027] Further in accordance with a preferred embodiment of the present invention the invention includes a probe including the DNA.

[0028] Still further in accordance with a preferred embodiment of the present invention the invention includes a method of selectively detecting expression of at least one gene, including using the probe.

[0029] Additionally in accordance with a preferred embodiment of the present invention the invention includes a gene expression detection system including: the probe, and a gene expression detector functional to selectively detect expression of at least one gene.

[0030] Further in accordance with a preferred embodiment of the present invention the invention includes an anti-viral substance capable of neutralizing the RNA.

[0031] Still further in accordance with a preferred embodiment of the present invention the neutralizing includes complementarily binding the RNA.

[0032] Additionally in accordance with a preferred embodiment of the present invention the neutralizing includes immunologically neutralizing.

- [0033] Moreover in accordance with a preferred embodiment of the present invention the invention includes a method for anti-viral treatment including neutralizing the RNA.
- [0034] Further in accordance with a preferred embodiment of the present invention the neutralizing includes: synthesizing a complementary nucleic acid molecule, a nucleic sequence of which complementary nucleic acid molecule is a partial inversed-reversed sequence of the RNA, and transfecting host cells with the complementary nucleic acid molecule, thereby complementarily binding the RNA.
- [0035] Still further in accordance with a preferred embodiment of the present invention the neutralizing includes immuno-logically neutralizing.

#### **BRIEF DESCRIPTION OF DRAWINGS**

- [0036] Fig. 1 is a simplified diagram illustrating a mode by which viral genes of a novel group of viral genes of the present invention, modulate expression of known host target genes;
- [0037] Fig. 2 is a simplified block diagram illustrating a bioinformatic gene detection system capable of detecting genes of the novel group of genes of the present invention, which system is constructed and operative in accordance with a preferred embodiment of the present invention;

- [0038] Fig. 3 is a simplified flowchart illustrating operation of a mechanism for training of a computer system to recognize the novel genes of the present invention, which mechanism is constructed and operative in accordance with a preferred embodiment of the present invention;
- [0039] Fig. 4A is a simplified block diagram of a non-coding genomic sequence detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0040] Fig. 4B is a simplified flowchart illustrating operation of a non-coding genomic sequence detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0041] Fig. 5A is a simplified block diagram of a hairpin detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0042] Fig. 5B is a simplified flowchart illustrating operation of a hairpin detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0043] Fig. 6A is a simplified block diagram of a dicer-cut location detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0044] Fig. 6B is a simplified flowchart illustrating training of a

dicer-cut location detector constructed and operative in accordance with a preferred embodiment of the present invention;

[0045] Fig. 7A is a simplified block diagram of a target-gene binding-site detector constructed and operative in accordance with a preferred embodiment of the present invention;

[0046] Fig. 7B is a simplified flowchart illustrating operation of a target-gene binding-site detector constructed and operative in accordance with a preferred embodiment of the present invention;

[0047] Fig. 8 is a simplified flowchart illustrating operation of a function & utility analyzer constructed and operative in accordance with a preferred embodiment of the present invention;

[0048] Fig. 9 is a simplified diagram describing a novel bioinformatically detected group of regulatory genes, referred to here as Genomic Record (GR) genes, each of which encodes an "operon-like" cluster of novel miRNA-like genes, which in turn modulates expression of a plurality of target genes;

[0049] Fig. 10 is a block diagram illustrating different utilities of genes of a novel group of genes, and operons of a novel

group of operons, both of the present invention;

[0050] Figs. 11A and 11B are simplified diagrams, which when taken together illustrate a mode of gene therapy applicable to genes of the novel group of genes of the present invention;

[0051] Fig. 12A is an annotated sequence of EST72223 comprising novel gene GAM24 detected by the gene detection system of the present invention;

[0052] Figs. 12B and 12C are pictures of laboratory results, which when taken together demonstrate laboratory confirmation of expression of the bioinformatically detected novel gene GAM24 of Fig. 12A;

[0053] Fig. 12D provides pictures of laboratory results, which when taken together demonstrate further laboratory confirmation of expression of the bioinformatically detected novel gene GAM24 of Fig. 12A;

[0054] Fig. 13A is an annotated sequence of an EST7929020 comprising novel genes GAM23 and GAM25 detected by the gene detection system of the present invention;

[0055] Fig. 13B is a picture of laboratory results, which confirm expression of bioinformatically detected novel genes GAM23 and GAM25 of Fig. 13A;

[0056] Fig. 13C is a picture of laboratory results, which confirm

endogenous expression of bioinformatically detected novel gene GAM25 of Fig. 15A;

[0057] Fig. 14A is an annotated sequence of an EST1388749 comprising novel gene GAM26 detected by the gene detection system of the present invention;

[0058] Figs. 14B is a picture of laboratory results, which confirm expression of the bioinformatically detected novel gene GAM26 of Fig. 14A;

[0059] Figs. 15A through 3838D are schematic diagrams illustrating sequences, functions and utilities of 3815 specific viral genes of the novel group of viral regulatory genes of the present invention, detected using the bioinformatic gene detection system described hereinabove with reference to Figs. 1 through 8; and

[0060] Figs. 3839 through 90679 are schematic diagrams illustrating sequences, functions and utilities of 86841 specific viral genes of a group of novel regulatory "operon-like" viral genes of the present invention, detected using the bioinformatic gene detection system described hereinabove with reference to Figs. 9 through 14.

#### **BRIEF DESCRIPTION OF SEQUENCES**

[0061] A Sequence Listing of nucleotide sequences of the present invention designated SEQ ID:1 through SEQ ID:86841 is

attached to this application, enclosed in computer readable form on CD-ROM, and include nucleotide sequences of 3815 novel genes of the present invention and their respective gene-precursors, and of 79292 target binding sites of these novel genes.

#### **DETAILED DESCRIPTION**

[0062] Reference is now made to Fig. 1 which is a simplified diagram illustrating a mode by which genes of a novel group of genes of the present invention, modulate expression of known host target.

[0063] The novel genes of the present invention are micro RNA (miRNA)-like, regulatory RNA genes, modulating expression of known host target. This mode of modulation is common to other known miRNA genes, as described hereinabove with reference to the background of the invention section.

[0064] VGAM GENE and TARGET GENE are two human genes contained in the DNA of the human genome.

[0065] VGAM GENE encodes a VGAM PRECURSOR RNA. However, similar to other miRNA genes, and unlike most ordinary genes, its RNA, VGAM PRECURSOR RNA, does not encode a protein.

[0066] VGAM PRECURSOR RNA folds onto itself, forming VGAM



FOLDED PRECURSOR RNA. As Fig.8 illustrates, VGAM FOLDED PRECURSOR RNA forms a "hairpin structure", folding onto itself. As is well known in the art, this "hairpin structure", is typical genes of the miRNA genes, and is due to the fact that nucleotide sequence of the first half of the RNA of a gene in this group is an accurate or partial inversed-reversed sequence of the nucleotide sequence of its second half. By "inversed-reversed" is meant a sequence which is reversed and wherein each nucleotide is replaced by a complimentary nucleotide, as is well known in the art (e.g. ATGGC is the inversed-reversed sequence of GCCAT).

[0067] An enzyme complex, designated DICER COMPLEX, "dices" the VGAM FOLDED PRECURSOR RNA into a single stranded RNA segment, about 22 nucleotides long, designated VGAM RNA. As is known in the art, "dicing" of the hairpin structured RNA precursor into shorter RNA segments about 22 nucleotides long by a Dicer type enzyme is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins.

[0068] TARGET GENE encodes a corresponding messenger RNA, designated TARGET RNA. This TARGET RNA comprises 3 regions: a 5' untranslated region, a protein coding region

and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[0069] VGAM RNA binds complementarily a BINDING SITE, located on the 3'UTR segment of TARGET RNA. This complementarily binding is due to the fact that the nucleotide sequence of VGAM RNA is an accurate or partial inversed-reversed sequence of the nucleotide sequence of BINDING SITE.

[0070] The complimentary binding of VGAM RNA to BINDING SITE inhibits translation of TARGET RNA into TARGET PROTEIN. TARGET PROTEIN is therefore outlined by a broken line.

[0071] It is appreciated by one skilled in the art that the mode of transcriptional inhibition illustrated by Fig. 1 with specific reference to VGAM genes of the present invention, is in fact common to all other miRNA genes. A specific complimentary binding site has been demonstrated only for Lin-4 and Let-7. All the other 93 newly discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complimentary binding, although specific complimentary binding sites for these genes have not yet been found (Ruvkun G., "Perspective: Glimpses of a tiny RNA world", Science 294 ,779 (2001)). The present invention discloses a novel group of

genes, the VGAM genes, belonging to the miRNA genes group, and for which a specific and complementary binding has been determined.

[0072] Reference is now made to Fig. 2 which is a simplified block diagram illustrating a bioinformatic gene detection system capable of detecting genes of the novel group of genes of the present invention, which system is constructed and operative in accordance with a preferred embodiment of the present invention.

[0073] A centerpiece of the present invention is a bioinformatic gene detection engine 100, which is a preferred implementation of a mechanism capable of bioinformatically detecting genes of the novel group of genes of the present invention.

[0074] The function of the bioinformatic gene detection engine 100 is as follows: it receives three types of input, expressed RNA data 102, sequenced DNA data 104, and protein function data 106, performs a complex process of analysis of this data as elaborated below, and based on this analysis produces output of a bioinformatically detected group of novel genes designated 108.

[0075] Expressed RNA data 102 comprises published expressed sequence tags (EST) data, , published mRNA data, as well

as other sources of published RNA data. Sequenced DNA data 104 comprises alphanumeric data describing sequenced genomic data, which preferably includes annotation data such as location of known protein coding regions relative to the sequenced data. Protein function data 106 comprises scientific publications reporting studies which elucidated physiological function known proteins, and their connection, involvement and possible utility in treatment and diagnosis of various diseases. Expressed RNA data 102, sequenced DNA data 104 may preferably be obtained from data published by the National Center for Bioinformatics (NCBI) at the National Institute of Health (NIH), as well as from various other published data sources. Protein function data 106 may preferably be obtained from any one of numerous relevant published data sources, such as the Online Mendelian Inherited Disease In Man (OMIM) database developed by John Hopkins University, and also published by NCBI.

[0076] Prior to actual detection of bioinformatically detected novel genes 108 by the bioinformatic gene detection engine 100, a process of bioinformatic gene detection engine training & validation designated 110 takes place. This process uses the known miRNA genes as a training

set (some 200 such genes have been found to date using biological laboratory means), to train the bioinformatic gene detection engine 100 to bioinformatically recognize miRNA-like genes, and their respective potential target binding sites. Bioinformatic gene detection engine training & validation 110 is further describe hereinbelow with reference to Fig. 3.

[0077] The bioinformatic gene detection engine 100 comprises several modules which are preferably activated sequentially, and are described as follows:

[0078] A non-coding genomic sequence detector 112 operative to bioinformatically detect non-protein coding genomic sequences. The non-coding genomic sequence detector 112 is further described hereinbelow with reference to Figs. 4A and 4B.

[0079] A hairpin detector 114 operative to bioinformatically detect genomic "hairpin-shaped" sequences, similar to VGAM FOLDED PRECURSOR of Fig. 1. The hairpin detector 114 is further described hereinbelow with reference to Figs. 5A and 5B.

[0080] A dicer-cut location detector 116 operative to bioinformatically detect the location on a hairpin shaped sequence which is enzymatically cut by DICER COMPLEX of Fig. 1.

The dicer-cut location detector 116 is further described hereinbelow with reference to Fig. 6A.

[0081] A target-gene binding-site detector 118 operative to bioinformatically detect host target having binding sites, the nucleotide sequence of which is partially complementary to that of a given genomic sequence, such as a sequence cut by DICER COMPLEX of Fig. 1. The target-gene binding-site detector 118 is further described hereinbelow with reference to Figs. 7A and 7B.

[0082] A function & utility analyzer 120 operative to analyze function and utility of host target, in order to identify host target which have a significant clinical function and utility. The function & utility analyzer 120 is further described hereinbelow with reference to Fig. 8.

[0083] Hardware implementation of the bioinformatic gene detection engine 100 is important, since significant computing power is preferably required in order to perform the computation of bioinformatic gene detection engine 100 in reasonable time and cost. As an example, it is estimated that using one powerful 8-processor PC Server, over 30 months of computing time (at 24 hours per day) would be required in order to detect all miRNA genes in human EST data, and their respective binding sites.

[0084] For example, in order to address this challenge at reasonable time and cost, a preferred embodiment of the present invention may comprise a cluster of a large number of personal computers (PCs), such as 100 PCs (Pentium IV, 1.7GHz, with 40GB storage each), connected by Ethernet to several strong servers, such as 4 servers (2-CPU, Xeon 2.2GHz, with 200GB storage each), combined with an 8-processor server (8-CPU, Xeon 550Mhz w/ 8GB RAM) connected via 2 HBA fiber-channels to an EMC Clariion 100-disks, 3.6 Terabyte storage device. Additionally, preferably an efficient database computer program, such as Microsoft (TM) SQL-Server database computer program is used and is optimized to the specific requirements of bioinformatic gene detection engine 100. Furthermore, the PCs are preferably optimized to operate close to 100% CPU usage continuously, as is known in the art. Using suitable hardware and software may preferably reduce the required calculation time in the abovementioned example from 30 months to 20 days.

[0085] It is appreciated that the abovementioned hardware configuration is not meant to be limiting, and is given as an illustration only. The present invention may be implemented in a wide variety of hardware and software config-

urations.

[0086] The present invention discloses 3815 novel viral genes of the VGAM group of genes, which have been detected bioinformatically, as described hereinbelow with reference to Figs. 15 through 3838. Laboratory confirmation of 4 genes of the GAM group of genes is described hereinbelow with reference to Figs. 12 through 14.

[0087] Reference is now made to Fig. 3 which is a simplified flowchart illustrating operation of a mechanism for training of a computer system to recognize the novel genes of the present invention. This mechanism is a preferred implementation of the bioinformatic gene detection engine training & validation 110 described hereinabove with reference to Fig. 2.

[0088] Bioinformatic gene detection engine training & validation 110 of Fig. 2 begins by training the bioinformatic gene detection engine to recognize known miRNA genes, as designated by numeral 122. This training step comprises hairpin detector training & validation 124, further described hereinbelow with reference to Fig. 12 A, dicer-cut location detector training & validation 126, further described hereinbelow with reference to Fig. 6A and 6B, and target-gene binding-site detector training & validation



128, further described hereinbelow with reference to Fig. 7A.

[0089] Next, the bioinformatic gene detection engine 100 is used to bioinformatically detect sample novel genes, as designated by numeral 130. An example of a sample novel gene thus detected is described hereinbelow with reference to Fig. 12.

[0090] Finally, wet lab experiments are preferably conducted in order to validate expression and preferably function the sample novel genes detected by the bioinformatic gene detection engine 100 in the previous step. An example of wet-lab validation of the abovementioned sample novel gene bioinformatically detected by the system is described hereinbelow with reference to Figs. 13A and 13B.

[0091] Reference is now made to Fig. 4A which is a simplified block diagram of a preferred implementation of the non-coding genomic sequence detector 112 described hereinabove with reference to Fig. 2. Non-protein coding genomic sequence detector 112 of Fig. 2 preferably receives as input at least two types of published genomic data: expressed RNA data 102, including EST data and mRNA data, and sequenced DNA data 104. After its initial training, indicated by numeral 134, and based on the above-

mentioned input data, the non-protein coding genomic sequence detector 112 produces as output a plurality of non-protein coding genomic sequences 136. Preferred operation of the non-protein coding genomic sequence detector 112 is described hereinbelow with reference to Fig. 4B.

[0092] Reference is now made to Fig. 4B which is a simplified flowchart illustrating a preferred operation of the non-coding genomic sequence detector 112 of Fig. 2. Detection of non-protein coding genomic sequences to be further analyzed by the system generally preferably progresses in one of the following two paths.

[0093] A first path for detecting non-protein coding genomic sequences begins by receiving a plurality of known RNA sequences, such as EST data. Each RNA sequence is first compared to all known protein-coding sequences, in order to select only those RNA sequences which are non-protein coding. This can preferably be performed by BLAST comparison of the RNA sequence to known protein coding sequences. The abovementioned BLAST comparison to the DNA preferably also provides the localization of the RNA on the DNA.

[0094] Optionally, an attempt may be made to "expand" the non-

protein RNA sequences thus found, by searching for transcription start and end signals, upstream and downstream of location of the RNA on the DNA respectively, as is well known in the art.

[0095] A second path for detecting non-protein coding genomic sequences starts by receiving DNA sequences. The DNA sequences are parsed into non protein coding sequences, based on published DNA annotation data: extracting those DNA sequences which are between known protein coding sequences. Next, transcription start and end signals are sought. If such signals are found, and depending on their "strength", probable expressed non-protein coding genomic sequences are yielded.

[0096] Reference is now made to Fig. 5A which is a simplified block diagram of a preferred implementation of the hairpin detector 114 described hereinabove with reference to Fig. 2.

[0097] The goal of the hairpin detector 114 is to detect "hairpin" shaped genomic sequences, similar to those of known miRNA genes. As mentioned hereinabove with reference to Fig. 1, a "hairpin" genomic sequence refers to a genomic sequence which "folds onto itself" forming a hairpin like shape, due to the fact that nucleotide sequence of the

first half of the nucleotide sequence is an accurate or

[0098] The hairpin detector 114 of Fig. 2 receives as input a plurality of non-protein coding genomic sequences 136 of Fig. 4A, and after a phase of hairpin detector training & validation 124 of Fig. 3, is operative to detect and output "hairpin shaped" sequences found in the input expressed non-protein coding sequences, designated by numeral 138.

[0099] The phase of hairpin detector training & validation 124 is an iterative process of applying the hairpin detector 114 to known hairpin shaped miRNA genes, calibrating the hairpin detector 114 such that it identifies the training set of known hairpins, as well as sequences which are similar thereto. Preferred operation of the hairpin detector 114 is described hereinbelow with reference to Fig. 5B.

[0100] Reference is now made to Fig. 5B which is a simplified flowchart illustrating a preferred operation of the hairpin detector 114 of Fig. 2.

[0101] A hairpin structure is a two dimensional folding structure, resulting from the nucleotide sequence pattern: the nucleotide sequence of the first half of the hairpin sequence is an inversed-reversed sequence of the second half thereof. Different methodologies are known in the art for

detection of various two dimensional and three dimensional hairpin structures.

[0102] In a preferred embodiment of the present invention, the hairpin detector 114 initially calculates possible 2-dimensional (2D) folding patterns of a given one of the non-protein coding genomic sequences 136, preferably using a 2D folding algorithm based on free-energy calculation, such as the Zuker algorithm, as is well known in the art.

[0103] Next, the hairpin detector 114 analyzes the results of the 2D folding, in order to determine the presence, and location of hairpin structures. A 2D folding algorithm typically provides as output a listing of the base-pairing of the 2D folded shape, i.e. a listing of which all two pairs of nucleotides in the sequence which will bond. The goal of this second step, is to assess this base-pairing listing, in order to determine if it describes a hairpin type bonding pattern.

[0104] The hairpin detector 114 then assess those hairpin structures found by the previous step, comparing them to hairpins of known miRNA genes, using various parameters such as length, free-energy, amount and type of mismatches, etc. Only hairpins that bear statistically signifi-

cant resemblance of the population of hairpins of known miRNAs, according to the abovementioned parameters are accepted.

[0105] Lastly, the hairpin detector 114 attempts to select those hairpin structures which are as stable as the hairpins of know miRNA genes. This may be achieved in various manners. A preferred embodiment of the present invention utilizes the following methodology comprising three steps:

[0106] First, the hairpin detector 114 attempts to group potential hairpins into "families" of closely related hairpins. As is known in the art, a free-energy calculation algorithm, typically provides multiple "versions" each describing a different possible 2D folding pattern for the given genomic sequence, and the free energy of such possible folding. The hairpin detector 114 therefore preferably assesses all hairpins found on all "versions", grouping hairpins which appear in different versions, but which share near identical locations into a common "family" of hairpins. For example, all hairpins in different versions, the center of which is within 7 nucleotides of each other may preferably be grouped to a single "family".

[0107] Next, hairpin "families" are assessed, in order to select

only those families which represent hairpins that are as stable as those of known miRNA hairpins. For example, preferably only families which are represented in at least 65% of the free-energy calculation 2D folding versions, are considered stable.

[0108] Finally, an attempt is made to select the most suitable hairpin from each selected family. For example, preferably the hairpin which appears in more versions than other hairpins, and in versions the free-energy of which is lower, may be selected.

[0109] Reference is now made to Fig. 6A which is a simplified block diagram of a preferred implementation of the dicer-cut location detector 116 described hereinabove with reference to Fig. 2.

[0110] The goal of the dicer-cut location detector 116 is to detect the location in which DICER COMPLEX of Fig. 1, comprising the enzyme Dicer, would "dice" the given hairpin sequence, similar to VGAM FOLDED PRECURSOR RNA, yielding VGAM RNA both of Fig. 1.

[0111] The dicer-cut location detector 116 of Fig. 2 therefore receives as input a plurality of hairpins on genomic sequences 138 of Fig. 5A, which were calculated by the previous step, and after a phase of dicer-cut location detec-

tor training & validation 126 of Fig. 3, is operative to detect a respective plurality of dicer-cut sequences from hairpins 140, one for each hairpin.

[0112] In a preferred embodiment of the present invention, the dicer-cut location detector 116 preferably uses a combination of neural networks, Bayesian networks, Markovian modeling, and Support Vector Machines (SVMs) trained on the known dicer-cut locations of known miRNA genes, in order to detect dicer-cut locations. Dicer-cut location detector training & validation 126, which is further described hereinbelow with reference to Fig. 6B.

[0113] Reference is now made to Fig. 6 B which is a simplified flowchart illustrating a preferred implementation of dicer-cut location detector training & validation 126 of Fig. 3. Dicer-cut location detector 116 first preprocesses known miRNA hairpins and their respective dicer-cut locations, so as to be able to properly analyze them and train the detection system accordingly:

[0114] The folding pattern is calculated for each known miRNA, preferably based on free-energy calculation, and the size of the hairpin, the size of the loop at the center of the hairpin, and "bulges" (i.e. mismatched base-pairs) in the folded hairpin are noted.



[0115] The dicer-cut location, which is known for known miRNA genes, is noted relative to the above, as well as to the nucleotides in each location along the hairpin. Frequency of identity of nucleotides, and nucleotide-pairing, relative to their location in the hairpin, and relative to the known dicer-cut location in the known miRNA genes is analyzed and modeled.

[0116] Different techniques are well known in the art for analysis of existing pattern from a given "training set" of species belonging to a genus, which techniques are then capable, to a certain degree, to detect similar patterns in other species not belonging to the training-set genus. Such techniques include, but are not limited to neural networks, Bayesian networks, Support Vector Machines (SVM), Genetic Algorithms, Markovian modeling, and others, as is well known in the art.

[0117] Using such techniques, preferably a combination of several of the above techniques, the known hairpins are represented as a several different networks (such as neural, Bayesian, or SVM) input and output layers. Both nucleotide, and "bulge" (i.e. nucleotide pairing or mismatch) are represented for each position in the hairpin, at the input layer, and a corresponding true/false flag at each po-

sition, indicating whether it was diced by dicer at the output layer. Multiple networks are preferably used concurrently, and the results therefrom are integrated and further optimized. Markovian modeling may also be used to validate the results and enhance their accuracy. Finally, the bioinformatic detection of dicer-cut location of a sample novel is confirmed by wet-lab experimentation.

[0118] Reference is now made to Fig. 7A which is a simplified block diagram of a preferred implementation of the target-gene binding-site detector 118 described herein-above with reference to Fig. 2. The goal of the target-gene binding-site detector 118 is to detect a BINDING SITE of Fig. 1, located in an untranslated region of the RNA of a known gene, the nucleotide sequence of which BINDING SITE is at least partially complementary to that of a VGAM RNA of Fig. 1, thereby determining that the abovementioned known gene is a target gene of VGAM of Fig. 1.

[0119] The target-gene binding-site detector 118 of Fig. 2 therefore receives as input a plurality of dicer-cut sequences from hairpins 140 of Fig. 6A which were calculated by the previous step, and a plurality of potential target gene sequences 142 which derive sequence DNA data

104 of Fig. 2, and after a phase of target–gene binding–site detector training & validation 128 of Fig. 3, is operative to detect target–genes having binding site/s 144 the nucleotide sequence of which is at least partially complementary to that of each of the plurality of dicer–cut sequences from hairpins 140. Preferred operation of the target–gene binding–site detector is further described hereinbelow with reference to Fig. 7B.

[0120] Reference is now made to Fig. 7B which is a simplified flowchart illustrating a preferred operation of the target–gene binding–site detector 118 of Fig. 2. In a preferred embodiment of the present invention, the target–gene binding–site detector 118 first performs a BLAST comparison of the nucleotide sequence of each of the plurality of dicer–cut sequences from hairpins 140, to the potential target gene sequences 142, in order to find crude potential matches. Blast results are then filtered to results which are similar to those of known binding sites (e.g. binding sites of miRNA genes Lin–4 and Let–7 to target genes Lin–14, Lin–41, Lin 28 etc.). Next the binding site is expanded, checking if nucleotide sequenced immediately adjacent to the binding site found by BLAST, may improve the match. Suitable binding sites, then are computed for

free-energy and spatial structure. The results are analyzed, selecting only those binding sites, which have free-energy and spatial structure similar to that of known binding sites.

[0121] Reference is now made to Fig. 8 which is a simplified flowchart illustrating a preferred operation of the function & utility analyzer 120 described hereinabove with reference to Fig. 2. The goal of the function & utility analyzer 120 is to determine if a potential target gene is in fact a valid clinically useful target gene. Since a potential novel VGAM gene binding a binding site in the UTR of a target gene is understood to inhibit expression of that target gene, and if that target gene is shown to have a valid clinical utility, then in such a case it follows that the potential novel gene itself also has a valid useful function which is the opposite of that of the target gene.

[0122] The function & utility analyzer 120 preferably receives as input a plurality of potential novel target genes having binding-site/s 144, generated by the target-gene binding-site detector 118, both of Fig. 7A. Each potential gene, is evaluated as follows:

[0123] First the system first checks to see if the function of the potential target gene is scientifically well established.

Preferably, this can be achieved bioinformatically by searching various published data sources presenting information on known function of proteins. Many such data sources exist and are published as is well known in the art.

[0124] Next, for those target genes the function of which is scientifically known and is well documented, the system then checks if scientific research data exists which links them to known diseases. For example, a preferred embodiment of the present invention utilizes the OMIM(TM) database published by NCBI, which summarizes research publications relating to genes which have been shown to be associated with diseases.

[0125] Finally, the specific possible utility of the target gene is evaluated. While this process too may be facilitated by bioinformatic means, it might require human evaluation of published scientific research regarding the target gene, in order to determine the utility of the target gene to the diagnosis and or treatment of specific disease. Only potential novel genes, the target-genes of which have passed all three examinations, are accepted as novel genes.

[0126] Reference is now made to Fig. 9, which is a simplified diagram describing a novel bioinformatically detected group

of regulatory genes, referred to here as Genomic Record (GR) genes, that encode an "operon-like" cluster of novel miRNA-like genes, each modulating expression of a plurality of host target, the function and utility of which target genes is known.

[0127] GR GENE (Genomic Record Gene) is gene of a novel, bioinformatically detected group of regulatory, non protein coding, RNA genes. The method by which GR is detected is described hereinabove with reference to FIGS. 6–15.

[0128] GR GENE encodes an RNA molecule, typically several hundred nucleotides long, designated GR PRECURSOR RNA.

[0129] GR PRECURSOR RNA folds spatially, as illustrated by GR FOLDED PRECURSOR RNA, into a plurality of what is known in the art as "hair-pin" structures. The nucleotide sequence of GR PRECURSOR RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, thereby causing formation of a plurality of "hairpin" structures, as is well known in the art.

[0130] GR FOLDED PRECURSOR RNA is naturally processed by cellular enzymatic activity, into 3 separate hairpin shaped RNA segments, each corresponding to VGAM PRECURSOR

RNA of Fig. 1, designated VGAM1 PRECURSOR, VGAM2 PRECURSOR and VGAM3 PRECURSOR respectively.

[0131] The above mentioned VGAM precursors, are diced by Dicer of FIG. 1, yielding short RNA segments of about 22 nucleotides in length, each corresponding to VGAM RNA of FIG. 1, designated VGAM1, VGAM2 and VGAM3 respectively.

[0132] VGAM1, VGAM2 and VGAM3 each bind complementarily to binding sites located in untranslated regions of respective host target, designated VGAM1-TARGET RNA, VGAM2-TARGET RNA and VGAM3-TARGET RNA respectively. This binding inhibits translation of the respective target proteins designated VGAM1-TARGET PROTEIN, VGAM2-TARGET PROTEIN and VGAM3-TARGET PROTEIN respectively.

[0133] The structure of VGAM genes comprised in a GR GENE, and their mode of modulation of expression of their respective target genes is described hereinabove with reference to Fig. 1. The bioinformatic approach to detection of VGAM genes comprised in a GR GENE is described hereinabove with reference to Figs. 9 through 14.

[0134] The present invention discloses 90656 novel viral genes of the GR group of genes, which have been detected

bioinformatically, as described hereinbelow with reference to Figs. 15 through 90679. Laboratory confirmation of 3 genes of the GR group of genes is described hereinbelow with reference to Figs. 9A through 14.

[0135] In summary, the current invention discloses a very large number of novel viral GR genes, each of which encodes a plurality of VGAM genes, which in turn may modulate expression of a plurality of host target proteins.

[0136] Reference is now made to Fig. 10 which is a block diagram illustrating different utilities of genes of the novel group of genes of the present invention referred to here as VGAM genes and GR genes.

[0137] The present invention discloses a first plurality of novel genes referred to here as VGAM genes, and a second plurality of operon-like genes referred to here as GR genes, each of the GR genes encoding a plurality of VGAM genes. The present invention further discloses a very large number of known target-genes, which are bound by, and the expression of which is modulated by each of the novel genes of the present invention. Published scientific data referenced by the present invention provides specific, substantial, and credible evidence that the abovementioned target genes modulated by novel genes of the



present invention, are associated with various diseases. Specific novel genes of the present invention, target genes thereof and diseases associated therewith, are described hereinbelow with reference to Figs. 15 through 3838. It is therefore appreciated that a function of VGAM genes and GR genes of the present invention is modulation of expression of target genes related to known diseases, and that therefore utilities of novel genes of the present invention include diagnosis and treatment of the above-mentioned diseases. Fig. 10 describes various types of diagnostic and therapeutic utilities of novel genes of the present invention.

[0138] A utility of novel genes of the present invention is detection of VGAM genes and of GR genes. It is appreciated that since VGAM genes and GR genes modulate expression of disease related target genes, that detection of expression of VGAM genes in clinical scenarios associated with said diseases is a specific, substantial and credible utility. Diagnosis of novel genes of the present invention may preferably be implemented by RNA expression detection techniques, including but not limited to biochips, as is well known in the art. Diagnosis of expression of genes of the present invention may be useful for research pur-

poses, in order to further understand the connection between the novel genes of the present invention and the abovementioned related diseases, for disease diagnosis and prevention purposes, and for monitoring disease progress.

[0139] Another utility of novel genes of the present invention is anti-VGAM gene therapy, a mode of therapy which allows up regulation of a disease related target-gene of a novel VGAM gene of the present invention, by lowering levels of the novel VGAM gene which naturally inhibits expression of that target gene. This mode of therapy is particularly useful with respect to target genes which have been shown to be under-expressed in association with a specific disease. Anti-VGAM gene therapy is further discussed hereinbelow with reference to Figs. 11A and 11B.

[0140] A further utility of novel genes of the present invention is VGAM replacement therapy, a mode of therapy which achieves down regulation of a disease related target-gene of a novel VGAM gene of the present invention, by raising levels of the VGAM gene which naturally inhibits expression of that target gene. This mode of therapy is particularly useful with respect to target genes which have been shown to be over-expressed in association with a specific

disease. VGAM replacement therapy involves introduction of supplementary VGAM gene products into a cell, or stimulation of a cell to produce excess VGAM gene products. VGAM replacement therapy may preferably be achieved by transfecting cells with an artificial DNA molecule encoding a VGAM gene, which causes the cells to produce the VGAM gene product, as is well known in the art.

[0141] Yet a further utility of novel genes of the present invention is modified VGAM therapy. Disease conditions are likely to exist, in which a mutation in a binding site of a VGAM gene prevents natural VGAM gene to effectively bind inhibit a disease related target-gene, causing up regulation of that target gene, and thereby contributing to the disease pathology. In such conditions, a modified VGAM gene is designed which effectively binds the mutated VGAM binding site, i.e. is an effective anti-sense of the mutated VGAM binding site, and is introduced in disease effected cells. Modified VGAM therapy is preferably achieved by transfecting cells with an artificial DNA molecule encoding the modified VGAM gene, which causes the cells to produce the modified VGAM gene product, as is well known in the art.

[0142] An additional utility of novel genes of the present invention is induced cellular differentiation therapy. An aspect of the present invention is finding genes which determine cellular differentiation, as described hereinabove with reference to Fig. 11. Induced cellular differentiation therapy comprises transfection of cell with such VGAM genes thereby determining their differentiation as desired. It is appreciated that this approach may be widely applicable, inter alia as a means for auto transplantation harvesting cells of one cell-type from a patient, modifying their differentiation as desired, and then transplanting them back into the patient. It is further appreciated that this approach may also be utilized to modify cell differentiation in vivo, by transfecting cells in a genetically diseased tissue with a cell-differentiation determining VGAM gene, thus stimulating these cells to differentiate appropriately.

[0143] Reference is now made to Figs. 11A and 11B, simplified diagrams which when taken together illustrate anti-VGAM gene therapy mentioned hereinabove with reference to Fig. 10. A utility of novel genes of the present invention is anti-VGAM gene therapy, a mode of therapy which allows up regulation of a disease related target-gene of a novel VGAM gene of the present invention, by lowering levels of

the novel VGAM gene which naturally inhibits expression of that target gene. Fig. 11A shows a normal VGAM gene, inhibiting translation of a target gene of VGAM gene, by binding to a BINDING SITE found in an untranslated region of TARGET RNA, as described hereinabove with reference to Fig. 1.

[0144] Fig. 11B shows an example of anti-VGAM gene therapy. ANTI-VGAM RNA is short artificial RNA molecule the sequence of which is an anti-sense of VGAM RNA. Anti-VGAM treatment comprises transfecting diseased cells with ANTI-VGAM RNA, or with a DNA encoding thereof. The ANTI-VGAM RNA binds the natural VGAM RNA, thereby preventing binding of natural VGAM RNA to its BINDING SITE. This prevents natural translation inhibition of TARGET RNA by VGAM RNA, thereby up regulating expression of TARGET PROTEIN.

[0145] It is appreciated that anti-VGAM gene therapy is particularly useful with respect to target genes which have been shown to be under-expressed in association with a specific disease.

[0146] Reference is now made to Fig. 12A which is an annotated sequence of an EST comprising a novel gene detected by the gene detection system of the present invention. Fig.

12A shows the nucleotide sequence of a known human non-protein coding EST (Expressed Sequence Tag), identified as EST72223. It is appreciated that the sequence of this EST comprises sequences of one known miRNA gene, identified as MIR98, and of one novel GAM gene, referred to here as GAM24, detected by the bioinformatic gene detection system of the present invention, described hereinabove with reference to Fig. 2.

[0147] Reference is now made to Figs. 12B and 12C that are pictures of laboratory results, which when taken together demonstrate laboratory confirmation of expression of the bioinformatically detected novel gene of Fig. 12A. Reference is now made to Fig. 12B which is a Northern blot analysis of MIR-98 and EST72223 transcripts. MIR-98 and EST72223 were reacted with MIR-98 and GAM24 probes as indicated in the figure. It is appreciated that the probes of both MIR-98 and GAM24 reacted with EST72223, indicating that EST72223 contains the sequences of MIR-98 and of GAM24. It is further appreciated that the probe of GAM24 does not cross-react with MIR-98.

[0148] Reference is now made to Fig. 12C. A Northern blot analysis of EST72223 and MIR-98 transfections were performed, subsequently marking RNA by the MIR-98 and

GAM24 probes . Left, Northern reacted with MIR-98, Right, Northern reacted with GAM24. The molecular Sizes of EST72223, MIR-98 and GAM24 are indicated by arrows. Hela are control cells that have not been introduced to exogenous RNA. EST and MIR-98 Transfections are RNA obtained from Hela transfected with EST72223 and MIR-98, respectively. MIR-98 and EST are the transcripts used for the transfection experiment. The results indicate that EST72223, when transfected into Hela cells, is cut yielding known miRNA gene MIR-98 and novel miRNA gene GAM24.

[0149] Reference is now made to Fig. 12D, which is a Northern blot of a lysate experiment with MIR-98 and GAM24. Northern blot analysis of hairpins in EST72223 . Left, Northern reacted with predicted Mir-98 hairpin probe, Right, Northern reacted with predicted GAM24 hairpin probe. The molecular size of EST is indicated by arrow. The molecular sizes of Mir-98 and GAM24 are 80nt and 100nt, respectively as indicated by arrows. The 22nt molecular marker is indicated by arrow. 1-Hela lysate; 2-EST incubated 4h with Hela lysate; 3-EST without lysate; 4-Mir transcript incubated 4h with Hela lysate; 5-Mir transcript incubated overnight with Hela lysate; 6- Mir

transcript without lysate; 7-RNA extracted from Hela cells following transfection with Mir transcript.

[0150] Technical methods used in experiments, the results of which are depicted in Figs. 12B, 12C and 12D are as follows:

[0151] *Transcript preparations:* Digoxigenin (DIG) labeled transcripts were prepared from EST72223 (TIGER), MIR98 and predicted precursor hairpins by using a DIG RNA labeling kit (Roche Molecular Biochemicals) according to the manufacturer's protocol. Briefly, PCR products with T7 promoter at the 5' end or T3 promoter at the 3' end were prepared from each DNA in order to use it as a template to prepare sense and antisense transcripts, respectively. MIR-98 was amplified using EST72223 as a template with T7miR98 forward primer:

5'-TAATACGACTCACTATAGGGTGAGGTAGTAAGTTGTATTGTT-3' and T3miR98 reverse primer:

5'-AATTAACCCTCACTAAAGGGAAAGTAGTAAGTTGTATAGTT-3' EST72223 was amplified with T7-EST 72223 forward primer: 5'-TAATACGACTCACTATAGGCCCTTATTAGAGGATTCTGCT-3' and T3-EST72223 reverse

primer: 5'-AATTAACCCTCACTAAAGGTTTTTTTTTCCTGAGACAGAGT-3' Bet-4 was amplified using EST72223 as a



templet with Bet-4 forward primer:

5"-GAGGCAGGAGAATTGCTTGA- 3" and T3-EST72223 reverse

primer:5"-AATTAACCCTCACTAAAGGCCTGAGACAGAGTCTTGCTC-3" The PCR products were cleaned and used for DIG-labeled or unlabeled transcription reactions with the appropriate polymerase. For transfection experiments, CAP reaction was performed by using a mMessage mMachine kit (Ambion).

[0152] *Transfection procedure:* Transfection of Hela cells was performed by using TransMessenger reagent (Qiagen) according to the manufacture's protocol. Briefly, Hela cells were seeded to  $1-2 \times 10^6$  cells per plate a day before transfection. Two  $\mu\text{g}$  RNA transcripts were mixed with 8  $\mu\text{l}$  Enhancer in a final volume of 100  $\mu\text{l}$ , mixed and incubated at room temperature for 5 min. 16  $\mu\text{l}$  TransMessenger reagent was added to the RNA-Enhancer, mixed and incubated for additional 10 min. Cell plates were washed with sterile PBS twice and then incubated with the transfection mix diluted with 2.5 ml DMEM medium without serum. Cells were incubated with transfection mix for three hours under their normal growth condition (37°C and 5% CO<sub>2</sub>) before the transfection mix was removed and a fresh

DMEM medium containing serum was added to the cells. Cells were left to grow 48 hours before harvesting.

[0153] *Target RNA cleavage assay:* Cap-labeled target RNAs were generated using mMessage mMachine<sup>TM</sup> (Ambion). Capped RNA transcripts were preincubated at 30<sup>0</sup>C for 15 min in supplemented Hela S100 obtained from Computer Cell Culture, Mos, Belgium. After addition of all components, final concentrations were 100mM target RNA, 1m M ATP, 0.2mM GTP, 10U/ml RNasin, 30µg/ml creatine kinase, 25mM creatine phosphate, and 50% S100 extract. Incubation was continued for 4 hours to overnight. Cleavage reaction was stopped by the addition of 8 volumes of proteinase K buffer (200Mm Tris-Hcl, pH 7.5, 25m M EDTA, 300mM NaCl, and 2% SDS). Proteinase K, dissolved in 50mM Tris-HCl, pH 8, 5m M CaCl<sub>2</sub>, and 50% glycerol, was added to a final concentration of 0.6 mg/ml. Samples were subjected to phenol/chlorophorm extraction and kept frozen until analyzed by urea-TBE PAGE.

[0154] *Northern analysis:* RNAs were extracted from cells by using Tri-reagent according to the manufacture's protocol. The RNAs were dissolved in water and heated to 65<sup>0</sup>C to disrupt any association of the 25nt RNA with larger RNA molecules. RNAs were placed on ice and incubated for 30

min with PEG (MW=8000) in a final concentration of 5% and NaCl in a final concentration of 0.5M to precipitate high molecular weight nucleic acid. The RNAs were centrifuged at 10,000xg for 10 min to pellet the high molecular weight nucleic acid. The supernatant containing the low molecular weight RNAs was collected and three volumes of ethanol was added. The RNAs were placed at -200C for at least two hours and then centrifuged at 10,000xg for 10 min. The pellets were dissolved in Urea-TBE buffer (1Xtbe, 7M urea) for further analysis by a Northern blot.

[0155] RNA samples were boiled for 5 min before loading on 15%-8% polyacrylamide (19:1) gels containing 7M urea and 1xTBE. Gels were run in 1xTBE at a constant voltage of 300V and then transferred into a nylon membrane. The membrane was exposed to 3min ultraviolet light to cross link the RNAs to the membrane. Hybridization was performed overnight with DIG-labeled probes at 420C. Membranes were washed twice with SSCx2 and 0.2% SDS for 10 min. at 420C and then washed twice with SSCx0.5 for 5 min at room temperature. The membrane was then developed by using a DIG luminescent detection kit (Roche) using anti DIG and CSPD reaction, according to the manu-

facture"s protocol.

[0156] It is appreciated that the data presented in Figs. 12A, 12B, 12C and 12D, when taken together validate the function of the bioinformatic gene detection engine 100 of Fig. 2. Fig. 12A shows a novel GAM gene bioinformatically detected by the bioinformatic gene detection engine 100, and Figs. 12B, 12C and 12D show laboratory confirmation of the expression of this novel gene. This is in accord with the engine training and validation methodology described hereinabove with reference to Fig. 3.

[0157] Reference is now made to Fig. 13A which is an annotated sequence of an EST comprising a novel gene detected by the gene detection system of the present invention. Fig. 13A shows the nucleotide sequence of a known human non-protein coding EST (Expressed Sequence Tag), identified as EST 7929020. It is appreciated that the sequence of this EST comprises sequences of two novel GAM genes, referred to here as GAM23 and GAM25, detected by the bioinformatic gene detection system of the present invention, described hereinabove with reference to Fig. 2.

[0158] Reference is now made to Fig. 13B which presents pictures of laboratory results, that demonstrate laboratory confirmation of expression of the bioinformatically de-

tected novel gene of Fig. 13A. Northern blot analysis of hairpins in EST7929020. Left, Northern reacted with predicted GAM25 hairpin probe, Right, Northern reacted with predicted GAM23 hairpin probe. The molecular size of EST is indicated by arrow. The molecular sizes of GAM23 and GAM25 are 60nt, as indicated by arrow. The 22nt molecular marker is indicated by arrow. 1-Hela lysate; 2- EST incubated 4h with Hela lysate ; 3- EST incubated overnight with Hela lysate; 4-EST without lysate; 5-GAM transcript; 6- GAM 22nt marker;7-GAM PCR probe; 8-RNA from control Hela cells; 9-RNA extracted from Hela cells following transfection with EST.

[0159] Reference is now made to Fig. 13C which is a picture of a Northern blot confirming Endogenous expression of bioinformatically detected gene GAM25 of Fig. 13A from in Hela cells. Northern was reacted with a predicted GAM25 hairpin probe. The molecular size of EST7929020 is indicated. The molecular sizes of GAM25 is 58nt, as indicated. A 19nt DNA oligo molecular marker is indicated. Endogenous expression of GAM25 in Hela total RNA fraction and in S-100 fraction is indicated by arrows. 1-GAM25 transcript; 2- GAM25 DNA oligo marker; 3-RNA from control Hela cells; 4-RNA extracted from Hela cells

following transfection with EST; 5- RNA extracted from S-100 Hela lysate.

[0160] Reference is now made to Fig. 14A which is an annotated sequence of an EST comprising a novel gene detected by the gene detection system of the present invention. Fig. 14A shows the nucleotide sequence of a known human non-protein coding EST (Expressed Sequence Tag), identified as EST 1388749. It is appreciated that the sequence of this EST comprises sequence of a novel GAM gene, referred to here as GAM26, detected by the bioinformatic gene detection system of the present invention, described hereinabove with reference to Fig. 2.

[0161] Reference is now made to Fig. 14B which is a picture of Northern blot analysis, confirming expression of novel bioinformatically detected gene GAM26, and natural processing thereof from EST1388749. Northern reacted with predicted GAM26 hairpin probe. The molecular size of EST is indicated by arrow. The molecular sizes of GAM26 is 130nt, as indicated by arrow. The 22nt molecular marker is indicated by arrow. 1-Hela lysate; 2-EST incubated 4h with Hela lysate; 3- EST incubated overnight with Hela lysate; 4-EST without lysate; 5-GAM transcript; 6- GAM 22nt marker; 7-GAM PCR probe.

[0162] Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 15 (VGAM15) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0163] VGAM15 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM15 was detected is described hereinabove with reference to Figs. 2–8.

[0164] VGAM15 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Melanoplus sanguinipes* entomopoxvirus. VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0165] VGAM15 gene, herein designated VGAM GENE, encodes a VGAM15 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM15 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM15 precursor RNA is designated SEQ ID:1, and is provided hereinbelow with

reference to the sequence listing part.

[0166] VGAM15 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM15 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0167] An enzyme complex designated DICER COMPLEX, dices the VGAM15 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM15 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM15 RNA is designated SEQ ID:2, and is provided hereinbelow with reference to the sequence listing part.



[0168] VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0169] VGAM15 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM15 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM15 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0170] The complementary binding of VGAM15 RNA, herein designated VGAM RNA, to host target binding sites on VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM15 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0171] It is appreciated that VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM15 host target genes. The mRNA of each one of this plurality of VGAM15 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM15 RNA, herein designated VGAM

RNA, and which when bound by VGAM15 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM15 host target proteins.

[0172] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM15 gene, herein designated VGAM GENE, on one or more VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0173] It is yet further appreciated that a function of VGAM15 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM15 include diagnosis, prevention and

treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM15 correlate with, and may be deduced from, the identity of the host target genes which VGAM15 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [0174] Nucleotide sequences of the VGAM15 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM15 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM15 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM15 are further described hereinbelow with reference to Table 1.
- [0175] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM15 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0176] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 16 (VGAM16) viral gene, which modulates expres-

sion of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0177] VGAM16 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM16 was detected is described hereinabove with reference to Figs. 2–8.

[0178] VGAM16 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0179] VGAM16 gene, herein designated VGAM GENE, encodes a VGAM16 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM16 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM16 precursor RNA is designated SEQ ID:8, and is provided hereinbelow with reference to the sequence listing part.

[0180] VGAM16 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM16 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0181] An enzyme complex designated DICER COMPLEX, dices the VGAM16 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM16 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM16 RNA is designated SEQ ID:9, and is provided hereinbelow with reference to the sequence listing part.

[0182] VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM16 host target RNA, herein designated

VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0183] VGAM16 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM16 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM16 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in

the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0184] The complementary binding of VGAM16 RNA, herein designated VGAM RNA, to host target binding sites on VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM16 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0185] It is appreciated that VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM16 host target genes. The mRNA of each one of this plurality of VGAM16 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM16 RNA, herein designated VGAM RNA, and which when bound by VGAM16 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM16 host target proteins.

[0186] It is further appreciated by one skilled in the art that the



mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM16 gene, herein designated VGAM GENE, on one or more VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0187] It is yet further appreciated that a function of VGAM16 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM16 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM16 correlate with, and may be deduced from, the identity of the host target genes which VGAM16 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[0188] Nucleotide sequences of the VGAM16 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM16 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM16 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM16 are further described hereinbelow with reference to Table 1.

[0189] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM16 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0190] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 17 (VGAM17) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0191] VGAM17 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM17 was detected is described hereinabove with reference to Figs. 2–8.

[0192] VGAM17 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM17 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0193] VGAM17 gene, herein designated VGAM GENE, encodes a VGAM17 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM17 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM17 precursor RNA is designated SEQ ID:22, and is provided hereinbelow with reference to the sequence listing part.

[0194] VGAM17 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM17 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0195] An enzyme complex designated DICER COMPLEX, dices the VGAM17 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM17 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM17 RNA is designated SEQ ID:23, and is provided hereinbelow with reference to the sequence listing part.

[0196] VGAM17 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR re-

spectively.

[0197] VGAM17 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM17 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM17 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0198] The complementary binding of VGAM17 RNA, herein des-

ignated VGAM RNA, to host target binding sites on VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM17 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0199] It is appreciated that VGAM17 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM17 host target genes. The mRNA of each one of this plurality of VGAM17 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM17 RNA, herein designated VGAM RNA, and which when bound by VGAM17 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM17 host target proteins.

[0200] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM17 gene, herein designated VGAM GENE, on one or more VGAM17 host target gene, herein designated VGAM

HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0201] It is yet further appreciated that a function of VGAM17 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM17 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM17 correlate with, and may be deduced from, the identity of the host target genes which VGAM17 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0202] Nucleotide sequences of the VGAM17 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM17 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM17 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM17 are further described hereinbelow with reference to Table 1.

[0203] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM17 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0204] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 18 (VGAM18) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0205] VGAM18 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM18 was detected is described hereinabove with reference to Figs. 2-8.

[0206] VGAM18 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2.



VGAM18 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0207] VGAM18 gene, herein designated VGAM GENE, encodes a VGAM18 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM18 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM18 precursor RNA is designated SEQ ID:39, and is provided hereinbelow with reference to the sequence listing part.

[0208] VGAM18 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM18 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0209] An enzyme complex designated DICER COMPLEX, dices

the VGAM18 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM18 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM18 RNA is designated SEQ ID:40, and is provided hereinbelow with reference to the sequence listing part.

[0210] VGAM18 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM18 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM18 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0211] VGAM18 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM18 host target RNA,

herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM18 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM18 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0212] The complementary binding of VGAM18 RNA, herein designated VGAM RNA, to host target binding sites on VGAM18 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM18 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM18 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0213] It is appreciated that VGAM18 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM18 host target genes. The mRNA of each one of this plurality of VGAM18 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM18 RNA, herein designated VGAM RNA, and which when bound by VGAM18 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM18 host target proteins.

[0214] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM18 gene, herein designated VGAM GENE, on one or more VGAM18 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only

for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0215] It is yet further appreciated that a function of VGAM18 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM18 correlate with, and may be deduced from, the identity of the host target genes which VGAM18 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0216] Nucleotide sequences of the VGAM18 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM18 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM18 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM18 are further de-

scribed hereinbelow with reference to Table 1.

[0217] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM18 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0218] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 19 (VGAM19) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0219] VGAM19 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM19 was detected is described hereinabove with reference to Figs. 2-8.

[0220] VGAM19 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0221] VGAM19 gene, herein designated VGAM GENE, encodes a

VGAM19 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM19 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM19 precursor RNA is designated SEQ ID:65, and is provided hereinbelow with reference to the sequence listing part.

[0222] VGAM19 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM19 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0223] An enzyme complex designated DICER COMPLEX, dices the VGAM19 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM19 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM19 RNA is designated SEQ ID:66, and is provided hereinbelow with reference to the sequence listing part.

[0224] VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0225] VGAM19 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of



the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM19 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0226] The complementary binding of VGAM19 RNA, herein designated VGAM RNA, to host target binding sites on VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM19 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0227] It is appreciated that VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM19 host target genes. The mRNA of each one of this plurality of VGAM19 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM19 RNA, herein designated VGAM RNA, and which when bound by VGAM19 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM19 host target proteins.

[0228] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM19 gene, herein designated VGAM GENE, on one or more VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although spe-

cific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0229] It is yet further appreciated that a function of VGAM19 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM19 correlate with, and may be deduced from, the identity of the host target genes which VGAM19 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0230] Nucleotide sequences of the VGAM19 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM19 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM19 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM19 are further described hereinbelow with reference to Table 1.

[0231] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM19 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0232] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 20 (VGAM20) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0233] VGAM20 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM20 was detected is described hereinabove with reference to Figs. 2–8.

[0234] VGAM20 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0235] VGAM20 gene, herein designated VGAM GENE, encodes a VGAM20 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM20 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a pro-

tein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM20 precursor RNA is designated SEQ ID:79, and is provided hereinbelow with reference to the sequence listing part.

[0236] VGAM20 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM20 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0237] An enzyme complex designated DICER COMPLEX, dices the VGAM20 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM20 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM20 RNA is designated SEQ ID:80, and is provided hereinbelow with reference to the sequence listing part.

[0238] VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0239] VGAM20 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM20 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0240] The complementary binding of VGAM20 RNA, herein designated VGAM RNA, to host target binding sites on VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM20 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0241] It is appreciated that VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM20 host target genes. The mRNA of each one of this plurality of VGAM20 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM20 RNA, herein designated VGAM RNA, and which when bound by VGAM20 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM20 host target proteins.

[0242] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM20 gene, herein designated VGAM GENE, on one or more VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0243] It is yet further appreciated that a function of VGAM20 is



inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM20 correlate with, and may be deduced from, the identity of the host target genes which VGAM20 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0244] Nucleotide sequences of the VGAM20 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM20 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM20 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM20 are further described hereinbelow with reference to Table 1.

[0245] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM20 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0246] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 21 (VGAM21) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0247] VGAM21 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM21 was detected is described hereinabove with reference to Figs. 2–8.

[0248] VGAM21 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM21 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0249] VGAM21 gene, herein designated VGAM GENE, encodes a VGAM21 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM21 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM21 precursor RNA is designated SEQ ID:95, and is provided hereinbelow with reference to the sequence listing part.

[0250] VGAM21 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM21 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0251] An enzyme complex designated DICER COMPLEX, dices the VGAM21 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM21 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM21 RNA is designated SEQ ID:96, and is provided hereinbelow with reference to the sequence listing part.

[0252] VGAM21 host target gene, herein designated VGAM HOST

TARGET GENE, encodes a corresponding messenger RNA, VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0253] VGAM21 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM21 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM21 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0254] The complementary binding of VGAM21 RNA, herein designated VGAM RNA, to host target binding sites on VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM21 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0255] It is appreciated that VGAM21 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM21 host target genes. The mRNA of each one of this plurality of VGAM21 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM21 RNA, herein designated VGAM RNA, and which when bound by VGAM21 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM21 host target proteins.

[0256] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM21 gene, herein designated VGAM GENE, on one or more VGAM21 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0257] It is yet further appreciated that a function of VGAM21 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM21 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Spe-

cific functions, and accordingly utilities, of VGAM21 correlate with, and may be deduced from, the identity of the host target genes which VGAM21 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [0258] Nucleotide sequences of the VGAM21 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM21 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM21 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM21 are further described hereinbelow with reference to Table 1.
- [0259] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM21 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0260] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 22 (VGAM22) viral gene, which modulates expression of respective host target genes thereof, the function

and utility of which host target genes is known in the art.

[0261] VGAM22 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM22 was detected is described hereinabove with reference to Figs. 2–8.

[0262] VGAM22 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM22 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0263] VGAM22 gene, herein designated VGAM GENE, encodes a VGAM22 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM22 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM22 precursor RNA is designated SEQ ID:113, and is provided hereinbelow with reference to the sequence listing part.

[0264] VGAM22 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM22 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.



As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0265] An enzyme complex designated DICER COMPLEX, dices the VGAM22 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM22 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM22 RNA is designated SEQ ID:114, and is provided hereinbelow with reference to the sequence listing part.

[0266] VGAM22 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is

typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0267] VGAM22 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM22 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM22 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these

host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0268] The complementary binding of VGAM22 RNA, herein designated VGAM RNA, to host target binding sites on VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM22 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0269] It is appreciated that VGAM22 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM22 host target genes. The mRNA of each one of this plurality of VGAM22 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM22 RNA, herein designated VGAM RNA, and which when bound by VGAM22 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM22 host target proteins.

[0270] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM22 gene, herein designated VGAM GENE, on one or more VGAM22 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0271] It is yet further appreciated that a function of VGAM22 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM22 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM22 correlate with, and may be deduced from, the identity of the host target genes which VGAM22 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [0272] Nucleotide sequences of the VGAM22 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM22 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM22 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM22 are further described hereinbelow with reference to Table 1.
- [0273] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM22 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0274] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 23 (VGAM23) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [0275] VGAM23 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM23 was detected is described

hereinabove with reference to Figs. 2–8.

[0276] VGAM23 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0277] VGAM23 gene, herein designated VGAM GENE, encodes a VGAM23 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM23 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM23 precursor RNA is designated SEQ ID:121, and is provided hereinbelow with reference to the sequence listing part.

[0278] VGAM23 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM23 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0279] An enzyme complex designated DICER COMPLEX, dices the VGAM23 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM23 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM23 RNA is designated SEQ ID:122, and is provided hereinbelow with reference to the sequence listing part.

[0280] VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0281] VGAM23 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM23 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0282] The complementary binding of VGAM23 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM23 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0283] It is appreciated that VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM23 host target genes. The mRNA of each one of this plurality of VGAM23 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM23 RNA, herein designated VGAM RNA, and which when bound by VGAM23 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM23 host target proteins.

[0284] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM23 gene, herein designated VGAM GENE, on one or more VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known

non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0285] It is yet further appreciated that a function of VGAM23 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM23 correlate with, and may be deduced from, the identity of the host target genes which VGAM23 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0286] Nucleotide sequences of the VGAM23 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM23 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM23 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM23 are further described hereinbelow with reference to Table 1.

[0287] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM23 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0288] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 24 (VGAM24) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0289] VGAM24 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM24 was detected is described hereinabove with reference to Figs. 2-8.

[0290] VGAM24 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM24 host target gene, herein desig-

nated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0291] VGAM24 gene, herein designated VGAM GENE, encodes a VGAM24 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM24 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM24 precursor RNA is designated SEQ ID:135, and is provided hereinbelow with reference to the sequence listing part.

[0292] VGAM24 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM24 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0293] An enzyme complex designated DICER COMPLEX, dices the VGAM24 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM24 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM24 RNA is designated SEQ ID:136, and is provided hereinbelow with reference to the sequence listing part.

[0294] VGAM24 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0295] VGAM24 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM24 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM24 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0296] The complementary binding of VGAM24 RNA, herein designated VGAM RNA, to host target binding sites on VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM24 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0297] It is appreciated that VGAM24 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM24 host target genes. The mRNA of each one of this plurality of VGAM24 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM24 RNA, herein designated VGAM RNA, and which when bound by VGAM24 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM24 host target proteins.

[0298] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM24 gene, herein designated VGAM GENE, on one or more VGAM24 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and

Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0299] It is yet further appreciated that a function of VGAM24 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM24 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM24 correlate with, and may be deduced from, the identity of the host target genes which VGAM24 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0300] Nucleotide sequences of the VGAM24 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM24 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM24 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM24 are further described hereinbelow with reference to Table 1.



[0301] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM24 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0302] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 25 (VGAM25) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0303] VGAM25 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM25 was detected is described hereinabove with reference to Figs. 2-8.

[0304] VGAM25 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM25 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0305] VGAM25 gene, herein designated VGAM GENE, encodes a VGAM25 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM25 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM25 precursor RNA is designated SEQ ID:139, and is provided hereinbelow with reference to the sequence listing part.

[0306] VGAM25 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM25 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0307] An enzyme complex designated DICER COMPLEX, dices the VGAM25 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM25 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM25 RNA is designated SEQ ID:140, and is provided hereinbelow with reference to the sequence listing part.

[0308] VGAM25 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0309] VGAM25 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding

sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM25 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0310] The complementary binding of VGAM25 RNA, herein designated VGAM RNA, to host target binding sites on VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM25 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0311] It is appreciated that VGAM25 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM25 host target genes. The mRNA of each one of this plurality of VGAM25 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM25 RNA, herein designated VGAM RNA, and which when bound by VGAM25 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM25 host target proteins.

[0312] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM25 gene, herein designated VGAM GENE, on one or more VGAM25 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA

genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0313] It is yet further appreciated that a function of VGAM25 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM25 correlate with, and may be deduced from, the identity of the host target genes which VGAM25 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0314] Nucleotide sequences of the VGAM25 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM25 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM25 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM25 are further described hereinbelow with reference to Table 1.

[0315] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM25 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0316] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 26 (VGAM26) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0317] VGAM26 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM26 was detected is described hereinabove with reference to Figs. 2–8.

[0318] VGAM26 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0319] VGAM26 gene, herein designated VGAM GENE, encodes a VGAM26 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM26 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to

the nucleotide sequence of VGAM26 precursor RNA is designated SEQ ID:151, and is provided hereinbelow with reference to the sequence listing part.

[0320] VGAM26 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM26 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0321] An enzyme complex designated DICER COMPLEX, dices the VGAM26 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM26 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM26 RNA is designated SEQ ID:152, and is



provided hereinbelow with reference to the sequence listing part.

[0322] VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0323] VGAM26 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM26 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting VGAM26 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0324] The complementary binding of VGAM26 RNA, herein designated VGAM RNA, to host target binding sites on VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM26 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0325] It is appreciated that VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM26 host target genes. The mRNA of each one of this plurality of VGAM26 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM26 RNA, herein designated VGAM RNA, and which when bound by VGAM26 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM26 host target proteins.

[0326] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM26 gene, herein designated VGAM GENE, on one or more VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0327] It is yet further appreciated that a function of VGAM26 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM26 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM26 correlate with, and may be deduced from, the identity of the host target genes which VGAM26 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0328] Nucleotide sequences of the VGAM26 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM26 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM26 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM26 are further described hereinbelow with reference to Table 1.

[0329] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM26 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0330] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 27 (VGAM27) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0331] VGAM27 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM27 was detected is described hereinabove with reference to Figs. 2–8.

[0332] VGAM27 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0333] VGAM27 gene, herein designated VGAM GENE, encodes a VGAM27 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM27 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM27 precursor RNA is designated SEQ ID:164, and is provided hereinbelow with reference to the sequence listing part.

[0334] VGAM27 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM27 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0335] An enzyme complex designated DICER COMPLEX, dices the VGAM27 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM27 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM27 RNA is designated SEQ ID:165, and is provided hereinbelow with reference to the sequence listing part.

[0336] VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA,

VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0337] VGAM27 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM27 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM27 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM27 host target RNA, herein

designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0338] The complementary binding of VGAM27 RNA, herein designated VGAM RNA, to host target binding sites on VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM27 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0339] It is appreciated that VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM27 host target genes. The mRNA of each one of this plurality of VGAM27 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM27 RNA, herein designated VGAM RNA, and which when bound by VGAM27 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM27 host target proteins.

[0340] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM27 gene, herein designated VGAM GENE, on one or more VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0341] It is yet further appreciated that a function of VGAM27 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM27 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM27 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM27 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0342] Nucleotide sequences of the VGAM27 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM27 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM27 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM27 are further described hereinbelow with reference to Table 1.

[0343] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM27 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0344] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 28 (VGAM28) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

- [0345] VGAM28 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM28 was detected is described hereinabove with reference to Figs. 2–8.
- [0346] VGAM28 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [0347] VGAM28 gene, herein designated VGAM GENE, encodes a VGAM28 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM28 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM28 precursor RNA is designated SEQ ID:179, and is provided hereinbelow with reference to the sequence listing part.
- [0348] VGAM28 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM28 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0349] An enzyme complex designated DICER COMPLEX, dices the VGAM28 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM28 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM28 RNA is designated SEQ ID:180, and is provided hereinbelow with reference to the sequence listing part.

[0350] VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untrans-

lated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0351] VGAM28 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM28 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR re-

gion, the 5UTR region, or in both 3UTR and 5UTR regions.

[0352] The complementary binding of VGAM28 RNA, herein designated VGAM RNA, to host target binding sites on VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM28 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0353] It is appreciated that VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM28 host target genes. The mRNA of each one of this plurality of VGAM28 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM28 RNA, herein designated VGAM RNA, and which when bound by VGAM28 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM28 host target proteins.

[0354] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM28 gene, herein designated VGAM GENE, on one or more VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0355] It is yet further appreciated that a function of VGAM28 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM28 correlate with, and may be deduced from, the identity of the host target genes which VGAM28 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [0356] Nucleotide sequences of the VGAM28 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM28 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM28 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM28 are further described hereinbelow with reference to Table 1.
- [0357] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM28 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0358] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 29 (VGAM29) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [0359] VGAM29 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM29 was detected is described hereinabove with reference to Figs. 2-8.



[0360] VGAM29 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0361] VGAM29 gene, herein designated VGAM GENE, encodes a VGAM29 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM29 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM29 precursor RNA is designated SEQ ID:188, and is provided hereinbelow with reference to the sequence listing part.

[0362] VGAM29 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM29 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[0363] An enzyme complex designated DICER COMPLEX, dices the VGAM29 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM29 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM29 RNA is designated SEQ ID:189, and is provided hereinbelow with reference to the sequence listing part.

[0364] VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0365] VGAM29 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM29 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0366] The complementary binding of VGAM29 RNA, herein designated VGAM RNA, to host target binding sites on VGAM29 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM29 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0367] It is appreciated that VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM29 host target genes. The mRNA of each one of this plurality of VGAM29 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM29 RNA, herein designated VGAM RNA, and which when bound by VGAM29 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM29 host target proteins.

[0368] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM29 gene, herein designated VGAM GENE, on one or more VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0369] It is yet further appreciated that a function of VGAM29 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM29 correlate with, and may be deduced from, the identity of the host target genes which VGAM29 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0370] Nucleotide sequences of the VGAM29 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM29 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM29 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM29 are further described hereinbelow with reference to Table 1.

[0371] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM29 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0372] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 30 (VGAM30) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0373] VGAM30 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM30 was detected is described hereinabove with reference to Figs. 2-8.

[0374] VGAM30 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[0375] VGAM30 gene, herein designated VGAM GENE, encodes a VGAM30 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM30 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM30 precursor RNA is designated SEQ ID:203, and is provided hereinbelow with reference to the sequence listing part.

[0376] VGAM30 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM30 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0377] An enzyme complex designated DICER COMPLEX, dices the VGAM30 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM30 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM30 RNA is designated SEQ ID:204, and is provided hereinbelow with reference to the sequence listing part.

[0378] VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0379] VGAM30 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide



sequence of VGAM30 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM30 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0380] The complementary binding of VGAM30 RNA, herein designated VGAM RNA, to host target binding sites on VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM30 host target protein, herein designated VGAM

HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0381] It is appreciated that VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM30 host target genes. The mRNA of each one of this plurality of VGAM30 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM30 RNA, herein designated VGAM RNA, and which when bound by VGAM30 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM30 host target proteins.

[0382] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM30 gene, herein designated VGAM GENE, on one or more VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0383] It is yet further appreciated that a function of VGAM30 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM30 correlate with, and may be deduced from, the identity of the host target genes which VGAM30 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0384] Nucleotide sequences of the VGAM30 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM30 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM30 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM30 are further described hereinbelow with reference to Table 1.

[0385] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM30 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0386] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 31 (VGAM31) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0387] VGAM31 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM31 was detected is described hereinabove with reference to Figs. 2-8.

[0388] VGAM31 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0389] VGAM31 gene, herein designated VGAM GENE, encodes a VGAM31 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM31 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM31 precursor RNA is designated SEQ ID:221, and is provided hereinbelow with reference to the sequence listing part.

[0390] VGAM31 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM31 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0391] An enzyme complex designated DICER COMPLEX, dices the VGAM31 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM31 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM31 RNA is designated SEQ ID:222, and is provided hereinbelow with reference to the sequence listing part.

[0392] VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0393] VGAM31 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM31 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target

binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM31 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0394] The complementary binding of VGAM31 RNA, herein designated VGAM RNA, to host target binding sites on VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM31 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0395] It is appreciated that VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM31 host target genes. The mRNA of each one of this plurality of VGAM31 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM31 RNA, herein designated VGAM RNA, and which when bound by VGAM31 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM31 host target proteins.

[0396] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM31 gene, herein designated VGAM GENE, on one or more VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective:



Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0397] It is yet further appreciated that a function of VGAM31 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM31 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM31 correlate with, and may be deduced from, the identity of the host target genes which VGAM31 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0398] Nucleotide sequences of the VGAM31 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM31 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM31 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM31 are further described hereinbelow with reference to Table 1.

[0399] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM31 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[0400] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 32 (VGAM32) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0401] VGAM32 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM32 was detected is described hereinabove with reference to Figs. 2–8.

[0402] VGAM32 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0403] VGAM32 gene, herein designated VGAM GENE, encodes a VGAM32 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM32 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM32 precursor RNA is

designated SEQ ID:225, and is provided hereinbelow with reference to the sequence listing part.

[0404] VGAM32 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM32 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0405] An enzyme complex designated DICER COMPLEX, dices the VGAM32 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM32 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM32 RNA is designated SEQ ID:226, and is provided hereinbelow with reference to the sequence list-

ing part.

[0406] VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0407] VGAM32 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM32 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing VGAM32 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0408] The complementary binding of VGAM32 RNA, herein designated VGAM RNA, to host target binding sites on VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM32 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0409] It is appreciated that VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM32 host target genes. The mRNA of each one of this plurality of VGAM32 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM32 RNA, herein designated VGAM RNA, and which when bound by VGAM32 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM32 host target proteins.

[0410] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM32 gene, herein designated VGAM GENE, on one or more VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0411] It is yet further appreciated that a function of VGAM32 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM32 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM32 correlate with, and may be deduced from, the identity of the host target genes which VGAM32 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0412] Nucleotide sequences of the VGAM32 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM32 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM32 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM32 are further described hereinbelow with reference to Table 1.

[0413] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM32 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0414] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 33 (VGAM33) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0415] VGAM33 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM33 was detected is described hereinabove with reference to Figs. 2–8.

[0416] VGAM33 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0417] VGAM33 gene, herein designated VGAM GENE, encodes a VGAM33 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM33 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM33 precursor RNA is designated SEQ ID:262, and is provided hereinbelow with reference to the sequence listing part.

[0418] VGAM33 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM33 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0419] An enzyme complex designated DICER COMPLEX, dices the VGAM33 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM33 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM33 RNA is designated SEQ ID:263, and is provided hereinbelow with reference to the sequence listing part.

[0420] VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM33 host target RNA, herein designated VGAM HOST

TARGET RNA. VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0421] VGAM33 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM33 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM33 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appre-

ciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0422] The complementary binding of VGAM33 RNA, herein designated VGAM RNA, to host target binding sites on VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM33 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0423] It is appreciated that VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM33 host target genes. The mRNA of each one of this plurality of VGAM33 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM33 RNA, herein designated VGAM RNA, and which when bound by VGAM33 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM33 host target proteins.

[0424] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM33 gene, herein designated VGAM GENE, on one or more VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0425] It is yet further appreciated that a function of VGAM33 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM33 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM33 correlate with, and may be deduced from, the

identity of the host target genes which VGAM33 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0426] Nucleotide sequences of the VGAM33 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM33 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM33 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM33 are further described hereinbelow with reference to Table 1.

[0427] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM33 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0428] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 34 (VGAM34) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0429] VGAM34 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM34 was detected is described hereinabove with reference to Figs. 2–8.

[0430] VGAM34 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0431] VGAM34 gene, herein designated VGAM GENE, encodes a VGAM34 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM34 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM34 precursor RNA is designated SEQ ID:268, and is provided hereinbelow with reference to the sequence listing part.

[0432] VGAM34 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM34 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0433] An enzyme complex designated DICER COMPLEX, dices the VGAM34 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM34 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM34 RNA is designated SEQ ID:269, and is provided hereinbelow with reference to the sequence listing part.

[0434] VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated

region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0435] VGAM34 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM34 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM34 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[0436] The complementary binding of VGAM34 RNA, herein designated VGAM RNA, to host target binding sites on VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM34 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0437] It is appreciated that VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM34 host target genes. The mRNA of each one of this plurality of VGAM34 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM34 RNA, herein designated VGAM RNA, and which when bound by VGAM34 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM34 host target proteins.

[0438] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM34 gene, herein designated VGAM GENE, on one or

more VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0439] It is yet further appreciated that a function of VGAM34 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM34 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM34 correlate with, and may be deduced from, the identity of the host target genes which VGAM34 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0440] Nucleotide sequences of the VGAM34 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM34 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM34 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM34 are further described hereinbelow with reference to Table 1.

[0441] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM34 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0442] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 35 (VGAM35) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0443] VGAM35 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM35 was detected is described hereinabove with reference to Figs. 2-8.

[0444] VGAM35 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Alcelaphine herpesvirus 1. VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0445] VGAM35 gene, herein designated VGAM GENE, encodes a VGAM35 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM35 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM35 precursor RNA is designated SEQ ID:298, and is provided hereinbelow with reference to the sequence listing part.

[0446] VGAM35 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM35 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0447] An enzyme complex designated DICER COMPLEX, dices the VGAM35 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM35 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM35 RNA is designated SEQ ID:299, and is provided hereinbelow with reference to the sequence listing part.

[0448] VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0449] VGAM35 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM35 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0450] The complementary binding of VGAM35 RNA, herein designated VGAM RNA, to host target binding sites on VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM35 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0451] It is appreciated that VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM35 host target genes. The mRNA of each one of this plurality of VGAM35 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM35 RNA, herein designated VGAM RNA, and which when bound by VGAM35 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM35 host target proteins.

[0452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM35 gene, herein designated VGAM GENE, on one or more VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0453] It is yet further appreciated that a function of VGAM35 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM35 correlate with, and may be deduced from, the identity of the host target genes which VGAM35 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0454] Nucleotide sequences of the VGAM35 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM35 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM35 folded precursor RNA, herein designated VGAM



FOLDED PRECURSOR RNA, of VGAM35 are further described hereinbelow with reference to Table 1.

[0455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM35 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0456] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 36 (VGAM36) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0457] VGAM36 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM36 was detected is described hereinabove with reference to Figs. 2-8.

[0458] VGAM36 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0459] VGAM36 gene, herein designated VGAM GENE, encodes a VGAM36 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM36 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM36 precursor RNA is designated SEQ ID:311, and is provided hereinbelow with reference to the sequence listing part.

[0460] VGAM36 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM36 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0461] An enzyme complex designated DICER COMPLEX, dices the VGAM36 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM36 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM36 RNA is designated SEQ ID:312, and is provided hereinbelow with reference to the sequence listing part.

[0462] VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0463] VGAM36 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA,

is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM36 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0464] The complementary binding of VGAM36 RNA, herein designated VGAM RNA, to host target binding sites on VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM36 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is

therefore outlined by a broken line.

[0465] It is appreciated that VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM36 host target genes. The mRNA of each one of this plurality of VGAM36 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM36 RNA, herein designated VGAM RNA, and which when bound by VGAM36 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM36 host target proteins.

[0466] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM36 gene, herein designated VGAM GENE, on one or more VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression

of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0467] It is yet further appreciated that a function of VGAM36 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM36 correlate with, and may be deduced from, the identity of the host target genes which VGAM36 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0468] Nucleotide sequences of the VGAM36 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM36 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM36 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM36 are further described hereinbelow with reference to Table 1.

[0469] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM36 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0470] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 37 (VGAM37) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0471] VGAM37 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM37 was detected is described hereinabove with reference to Figs. 2–8.

[0472] VGAM37 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0473] VGAM37 gene, herein designated VGAM GENE, encodes a VGAM37 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM37 precursor RNA, herein des-

ignated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM37 precursor RNA is designated SEQ ID:351, and is provided hereinbelow with reference to the sequence listing part.

[0474] VGAM37 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM37 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0475] An enzyme complex designated DICER COMPLEX, dices the VGAM37 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM37 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other



necessary proteins. A probable (over 28%) nucleotide sequence of VGAM37 RNA is designated SEQ ID:352, and is provided hereinbelow with reference to the sequence listing part.

[0476] VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0477] VGAM37 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II

and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM37 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0478] The complementary binding of VGAM37 RNA, herein designated VGAM RNA, to host target binding sites on VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM37 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0479] It is appreciated that VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM37 host target genes. The mRNA of

each one of this plurality of VGAM37 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM37 RNA, herein designated VGAM RNA, and which when bound by VGAM37 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM37 host target proteins.

[0480] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM37 gene, herein designated VGAM GENE, on one or more VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0481] It is yet further appreciated that a function of VGAM37 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM37 correlate with, and may be deduced from, the identity of the host target genes which VGAM37 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0482] Nucleotide sequences of the VGAM37 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM37 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM37 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM37 are further described hereinbelow with reference to Table 1.

[0483] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM37 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0484] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 38 (VGAM38) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0485] VGAM38 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM38 was detected is described hereinabove with reference to Figs. 2–8.

[0486] VGAM38 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM38 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0487] VGAM38 gene, herein designated VGAM GENE, encodes a VGAM38 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM38 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM38 precursor RNA is designated SEQ ID:366, and is provided hereinbelow with

reference to the sequence listing part.

[0488] VGAM38 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM38 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0489] An enzyme complex designated DICER COMPLEX, dices the VGAM38 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM38 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM38 RNA is designated SEQ ID:367, and is provided hereinbelow with reference to the sequence listing part.

[0490] VGAM38 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0491] VGAM38 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM38 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM38 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0492] The complementary binding of VGAM38 RNA, herein designated VGAM RNA, to host target binding sites on VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM38 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0493] It is appreciated that VGAM38 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM38 host target genes. The mRNA of each one of this plurality of VGAM38 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM38 RNA, herein designated VGAM



RNA, and which when bound by VGAM38 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM38 host target proteins.

[0494] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM38 gene, herein designated VGAM GENE, on one or more VGAM38 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0495] It is yet further appreciated that a function of VGAM38 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM38 include diagnosis, prevention and

treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM38 correlate with, and may be deduced from, the identity of the host target genes which VGAM38 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0496] Nucleotide sequences of the VGAM38 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM38 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM38 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM38 are further described hereinbelow with reference to Table 1.

[0497] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM38 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0498] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 39 (VGAM39) viral gene, which modulates expres-

sion of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0499] VGAM39 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM39 was detected is described hereinabove with reference to Figs. 2–8.

[0500] VGAM39 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0501] VGAM39 gene, herein designated VGAM GENE, encodes a VGAM39 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM39 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM39 precursor RNA is designated SEQ ID:394, and is provided hereinbelow with reference to the sequence listing part.

[0502] VGAM39 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM39 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0503] An enzyme complex designated DICER COMPLEX, dices the VGAM39 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM39 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM39 RNA is designated SEQ ID:395, and is provided hereinbelow with reference to the sequence listing part.

[0504] VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM39 host target RNA, herein designated

VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0505] VGAM39 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM39 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in

the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0506] The complementary binding of VGAM39 RNA, herein designated VGAM RNA, to host target binding sites on VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM39 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0507] It is appreciated that VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM39 host target genes. The mRNA of each one of this plurality of VGAM39 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM39 RNA, herein designated VGAM RNA, and which when bound by VGAM39 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM39 host target proteins.

[0508] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM39 gene, herein designated VGAM GENE, on one or more VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0509] It is yet further appreciated that a function of VGAM39 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM39 correlate with, and may be deduced from, the identity of the host target genes which VGAM39 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[0510] Nucleotide sequences of the VGAM39 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM39 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM39 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM39 are further described hereinbelow with reference to Table 1.

[0511] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM39 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0512] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 40 (VGAM40) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0513] VGAM40 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The



method by which VGAM40 was detected is described hereinabove with reference to Figs. 2–8.

[0514] VGAM40 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM40 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0515] VGAM40 gene, herein designated VGAM GENE, encodes a VGAM40 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM40 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM40 precursor RNA is designated SEQ ID:452, and is provided hereinbelow with reference to the sequence listing part.

[0516] VGAM40 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM40 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0517] An enzyme complex designated DICER COMPLEX, dices the VGAM40 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM40 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM40 RNA is designated SEQ ID:453, and is provided hereinbelow with reference to the sequence listing part.

[0518] VGAM40 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR re-

spectively.

[0519] VGAM40 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM40 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0520] The complementary binding of VGAM40 RNA, herein des-

ignated VGAM RNA, to host target binding sites on VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM40 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0521] It is appreciated that VGAM40 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM40 host target genes. The mRNA of each one of this plurality of VGAM40 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM40 RNA, herein designated VGAM RNA, and which when bound by VGAM40 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM40 host target proteins.

[0522] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM40 gene, herein designated VGAM GENE, on one or more VGAM40 host target gene, herein designated VGAM

HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0523] It is yet further appreciated that a function of VGAM40 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM40 correlate with, and may be deduced from, the identity of the host target genes which VGAM40 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0524] Nucleotide sequences of the VGAM40 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM40 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM40 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM40 are further described hereinbelow with reference to Table 1.

[0525] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM40 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0526] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 41 (VGAM41) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0527] VGAM41 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM41 was detected is described hereinabove with reference to Figs. 2-8.

[0528] VGAM41 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A.

VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0529] VGAM41 gene, herein designated VGAM GENE, encodes a VGAM41 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM41 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM41 precursor RNA is designated SEQ ID:455, and is provided hereinbelow with reference to the sequence listing part.

[0530] VGAM41 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM41 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0531] An enzyme complex designated DICER COMPLEX, dices

the VGAM41 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM41 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM41 RNA is designated SEQ ID:456, and is provided hereinbelow with reference to the sequence listing part.

[0532] VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0533] VGAM41 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM41 host target RNA,



herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM41 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM41 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0534] The complementary binding of VGAM41 RNA, herein designated VGAM RNA, to host target binding sites on VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM41 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM41 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0535] It is appreciated that VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM41 host target genes. The mRNA of each one of this plurality of VGAM41 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM41 RNA, herein designated VGAM RNA, and which when bound by VGAM41 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM41 host target proteins.

[0536] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM41 gene, herein designated VGAM GENE, on one or more VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only

for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0537] It is yet further appreciated that a function of VGAM41 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM41 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM41 correlate with, and may be deduced from, the identity of the host target genes which VGAM41 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0538] Nucleotide sequences of the VGAM41 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM41 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM41 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM41 are further de-

scribed hereinbelow with reference to Table 1.

[0539] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM41 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0540] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 42 (VGAM42) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0541] VGAM42 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM42 was detected is described hereinabove with reference to Figs. 2-8.

[0542] VGAM42 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0543] VGAM42 gene, herein designated VGAM GENE, encodes a

VGAM42 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM42 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM42 precursor RNA is designated SEQ ID:505, and is provided hereinbelow with reference to the sequence listing part.

[0544] VGAM42 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM42 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0545] An enzyme complex designated DICER COMPLEX, dices the VGAM42 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM42 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM42 RNA is designated SEQ ID:506, and is provided hereinbelow with reference to the sequence listing part.

[0546] VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0547] VGAM42 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of

the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM42 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0548] The complementary binding of VGAM42 RNA, herein designated VGAM RNA, to host target binding sites on VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM42 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0549] It is appreciated that VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM42 host target genes. The mRNA of each one of this plurality of VGAM42 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM42 RNA, herein designated VGAM RNA, and which when bound by VGAM42 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM42 host target proteins.

[0550] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM42 gene, herein designated VGAM GENE, on one or more VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although spe-



cific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0551] It is yet further appreciated that a function of VGAM42 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM42 correlate with, and may be deduced from, the identity of the host target genes which VGAM42 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0552] Nucleotide sequences of the VGAM42 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM42 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM42 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM42 are further described hereinbelow with reference to Table 1.

[0553] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM42 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0554] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 43 (VGAM43) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0555] VGAM43 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM43 was detected is described hereinabove with reference to Figs. 2–8.

[0556] VGAM43 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0557] VGAM43 gene, herein designated VGAM GENE, encodes a VGAM43 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM43 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a pro-

tein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM43 precursor RNA is designated SEQ ID:529, and is provided hereinbelow with reference to the sequence listing part.

[0558] VGAM43 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM43 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0559] An enzyme complex designated DICER COMPLEX, dices the VGAM43 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM43 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM43 RNA is designated SEQ ID:530, and is provided hereinbelow with reference to the sequence listing part.

[0560] VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0561] VGAM43 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM43 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM43 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0562] The complementary binding of VGAM43 RNA, herein designated VGAM RNA, to host target binding sites on VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM43 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0563] It is appreciated that VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM43 host target genes. The mRNA of each one of this plurality of VGAM43 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM43 RNA, herein designated VGAM RNA, and which when bound by VGAM43 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM43 host target proteins.

[0564] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM43 gene, herein designated VGAM GENE, on one or more VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0565] It is yet further appreciated that a function of VGAM43 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM43 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM43 correlate with, and may be deduced from, the identity of the host target genes which VGAM43 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0566] Nucleotide sequences of the VGAM43 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM43 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM43 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM43 are further described hereinbelow with reference to Table 1.

[0567] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM43 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0568] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 44 (VGAM44) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0569] VGAM44 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM44 was detected is described hereinabove with reference to Figs. 2–8.

[0570] VGAM44 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM44 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0571] VGAM44 gene, herein designated VGAM GENE, encodes a VGAM44 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM44 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM44 precursor RNA is designated SEQ ID:539, and is provided hereinbelow with reference to the sequence listing part.



[0572] VGAM44 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM44 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0573] An enzyme complex designated DICER COMPLEX, dices the VGAM44 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM44 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM44 RNA is designated SEQ ID:540, and is provided hereinbelow with reference to the sequence listing part.

[0574] VGAM44 host target gene, herein designated VGAM HOST

TARGET GENE, encodes a corresponding messenger RNA, VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0575] VGAM44 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM44 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM44 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0576] The complementary binding of VGAM44 RNA, herein designated VGAM RNA, to host target binding sites on VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM44 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0577] It is appreciated that VGAM44 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM44 host target genes. The mRNA of each one of this plurality of VGAM44 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM44 RNA, herein designated VGAM RNA, and which when bound by VGAM44 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM44 host target proteins.

[0578] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM44 gene, herein designated VGAM GENE, on one or more VGAM44 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0579] It is yet further appreciated that a function of VGAM44 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM44 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1.

Specific functions, and accordingly utilities, of VGAM44 correlate with, and may be deduced from, the identity of the host target genes which VGAM44 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [0580] Nucleotide sequences of the VGAM44 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM44 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM44 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM44 are further described hereinbelow with reference to Table 1.
- [0581] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM44 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0582] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 45 (VGAM45) viral gene, which modulates expression of respective host target genes thereof, the function

and utility of which host target genes is known in the art.

[0583] VGAM45 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM45 was detected is described hereinabove with reference to Figs. 2–8.

[0584] VGAM45 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0585] VGAM45 gene, herein designated VGAM GENE, encodes a VGAM45 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM45 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM45 precursor RNA is designated SEQ ID:559, and is provided hereinbelow with reference to the sequence listing part.

[0586] VGAM45 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM45 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0587] An enzyme complex designated DICER COMPLEX, dices the VGAM45 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM45 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM45 RNA is designated SEQ ID:560, and is provided hereinbelow with reference to the sequence listing part.

[0588] VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is

typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0589] VGAM45 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM45 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these



host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0590] The complementary binding of VGAM45 RNA, herein designated VGAM RNA, to host target binding sites on VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM45 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0591] It is appreciated that VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM45 host target genes. The mRNA of each one of this plurality of VGAM45 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM45 RNA, herein designated VGAM RNA, and which when bound by VGAM45 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM45 host target proteins.

[0592] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM45 gene, herein designated VGAM GENE, on one or more VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0593] It is yet further appreciated that a function of VGAM45 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM45 correlate with, and may be deduced from, the identity of the host target genes which VGAM45 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [0594] Nucleotide sequences of the VGAM45 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM45 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM45 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM45 are further described hereinbelow with reference to Table 1.
- [0595] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM45 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0596] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 46 (VGAM46) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [0597] VGAM46 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM46 was detected is described

hereinabove with reference to Figs. 2–8.

[0598] VGAM46 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM46 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0599] VGAM46 gene, herein designated VGAM GENE, encodes a VGAM46 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM46 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM46 precursor RNA is designated SEQ ID:572, and is provided hereinbelow with reference to the sequence listing part.

[0600] VGAM46 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM46 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0601] An enzyme complex designated DICER COMPLEX, dices the VGAM46 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM46 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM46 RNA is designated SEQ ID:573, and is provided hereinbelow with reference to the sequence listing part.

[0602] VGAM46 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0603] VGAM46 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM46 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0604] The complementary binding of VGAM46 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM46 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0605] It is appreciated that VGAM46 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM46 host target genes. The mRNA of each one of this plurality of VGAM46 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM46 RNA, herein designated VGAM RNA, and which when bound by VGAM46 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM46 host target proteins.

[0606] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM46 gene, herein designated VGAM GENE, on one or more VGAM46 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known

non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0607] It is yet further appreciated that a function of VGAM46 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM46 correlate with, and may be deduced from, the identity of the host target genes which VGAM46 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0608] Nucleotide sequences of the VGAM46 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM46 RNA, herein designated VGAM RNA, and a



schematic representation of the secondary folding of VGAM46 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM46 are further described hereinbelow with reference to Table 1.

[0609] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM46 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0610] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 47 (VGAM47) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0611] VGAM47 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM47 was detected is described hereinabove with reference to Figs. 2-8.

[0612] VGAM47 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM47 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[0613] VGAM47 gene, herein designated VGAM GENE, encodes a VGAM47 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM47 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM47 precursor RNA is designated SEQ ID:606, and is provided hereinbelow with reference to the sequence listing part.

[0614] VGAM47 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM47 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0615] An enzyme complex designated DICER COMPLEX, dices the VGAM47 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM47 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM47 RNA is designated SEQ ID:607, and is provided hereinbelow with reference to the sequence listing part.

[0616] VGAM47 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0617] VGAM47 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM47 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0618] The complementary binding of VGAM47 RNA, herein designated VGAM RNA, to host target binding sites on VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM47 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0619] It is appreciated that VGAM47 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM47 host target genes. The mRNA of each one of this plurality of VGAM47 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM47 RNA, herein designated VGAM RNA, and which when bound by VGAM47 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM47 host target proteins.

[0620] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM47 gene, herein designated VGAM GENE, on one or more VGAM47 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and

Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0621] It is yet further appreciated that a function of VGAM47 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM47 correlate with, and may be deduced from, the identity of the host target genes which VGAM47 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0622] Nucleotide sequences of the VGAM47 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM47 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM47 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM47 are further described hereinbelow with reference to Table 1.

[0623] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM47 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0624] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 48 (VGAM48) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0625] VGAM48 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM48 was detected is described hereinabove with reference to Figs. 2-8.

[0626] VGAM48 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM48 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0627] VGAM48 gene, herein designated VGAM GENE, encodes a VGAM48 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM48 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM48 precursor RNA is designated SEQ ID:623, and is provided hereinbelow with reference to the sequence listing part.

[0628] VGAM48 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM48 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0629] An enzyme complex designated DICER COMPLEX, dices the VGAM48 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM48 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM48 RNA is designated SEQ ID:624, and is provided hereinbelow with reference to the sequence listing part.

[0630] VGAM48 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0631] VGAM48 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM48 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding

sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM48 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0632] The complementary binding of VGAM48 RNA, herein designated VGAM RNA, to host target binding sites on VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM48 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0633] It is appreciated that VGAM48 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM48 host target genes. The mRNA of each one of this plurality of VGAM48 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM48 RNA, herein designated VGAM RNA, and which when bound by VGAM48 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM48 host target proteins.

[0634] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM48 gene, herein designated VGAM GENE, on one or more VGAM48 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA

genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0635] It is yet further appreciated that a function of VGAM48 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM48 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM48 correlate with, and may be deduced from, the identity of the host target genes which VGAM48 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0636] Nucleotide sequences of the VGAM48 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM48 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM48 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM48 are further described hereinbelow with reference to Table 1.

[0637] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM48 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0638] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 49 (VGAM49) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0639] VGAM49 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM49 was detected is described hereinabove with reference to Figs. 2–8.

[0640] VGAM49 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0641] VGAM49 gene, herein designated VGAM GENE, encodes a VGAM49 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM49 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to

the nucleotide sequence of VGAM49 precursor RNA is designated SEQ ID:643, and is provided hereinbelow with reference to the sequence listing part.

[0642] VGAM49 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM49 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0643] An enzyme complex designated DICER COMPLEX, dices the VGAM49 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM49 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM49 RNA is designated SEQ ID:644, and is

provided hereinbelow with reference to the sequence listing part.

[0644] VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0645] VGAM49 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM49 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting VGAM49 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0646] The complementary binding of VGAM49 RNA, herein designated VGAM RNA, to host target binding sites on VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM49 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0647] It is appreciated that VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM49 host target genes. The mRNA of each one of this plurality of VGAM49 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM49 RNA, herein designated VGAM RNA, and which when bound by VGAM49 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM49 host target proteins.

[0648] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM49 gene, herein designated VGAM GENE, on one or more VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0649] It is yet further appreciated that a function of VGAM49 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM49 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM49 correlate with, and may be deduced from, the identity of the host target genes which VGAM49 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0650] Nucleotide sequences of the VGAM49 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM49 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM49 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM49 are further described hereinbelow with reference to Table 1.

[0651] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM49 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0652] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 50 (VGAM50) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0653] VGAM50 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM50 was detected is described hereinabove with reference to Figs. 2–8.

[0654] VGAM50 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0655] VGAM50 gene, herein designated VGAM GENE, encodes a VGAM50 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM50 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM50 precursor RNA is designated SEQ ID:665, and is provided hereinbelow with reference to the sequence listing part.

[0656] VGAM50 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM50 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0657] An enzyme complex designated DICER COMPLEX, dices the VGAM50 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM50 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM50 RNA is designated SEQ ID:666, and is provided hereinbelow with reference to the sequence listing part.

[0658] VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA,

VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0659] VGAM50 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM50 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM50 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM50 host target RNA, herein

designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0660] The complementary binding of VGAM50 RNA, herein designated VGAM RNA, to host target binding sites on VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM50 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0661] It is appreciated that VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM50 host target genes. The mRNA of each one of this plurality of VGAM50 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM50 RNA, herein designated VGAM RNA, and which when bound by VGAM50 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM50 host target proteins.

[0662] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM50 gene, herein designated VGAM GENE, on one or more VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0663] It is yet further appreciated that a function of VGAM50 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM50 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM50

correlate with, and may be deduced from, the identity of the host target genes which VGAM50 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0664] Nucleotide sequences of the VGAM50 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM50 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM50 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM50 are further described hereinbelow with reference to Table 1.

[0665] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM50 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0666] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 51 (VGAM51) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[0667] VGAM51 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM51 was detected is described hereinabove with reference to Figs. 2–8.

[0668] VGAM51 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0669] VGAM51 gene, herein designated VGAM GENE, encodes a VGAM51 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM51 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM51 precursor RNA is designated SEQ ID:679, and is provided hereinbelow with reference to the sequence listing part.

[0670] VGAM51 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM51 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0671] An enzyme complex designated DICER COMPLEX, dices the VGAM51 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM51 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM51 RNA is designated SEQ ID:680, and is provided hereinbelow with reference to the sequence listing part.

[0672] VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untrans-

lated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0673] VGAM51 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM51 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR re-

gion, the 5UTR region, or in both 3UTR and 5UTR regions.

[0674] The complementary binding of VGAM51 RNA, herein designated VGAM RNA, to host target binding sites on VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM51 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0675] It is appreciated that VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM51 host target genes. The mRNA of each one of this plurality of VGAM51 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM51 RNA, herein designated VGAM RNA, and which when bound by VGAM51 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM51 host target proteins.

[0676] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM51 gene, herein designated VGAM GENE, on one or more VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0677] It is yet further appreciated that a function of VGAM51 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM51 correlate with, and may be deduced from, the identity of the host target genes which VGAM51 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [0678] Nucleotide sequences of the VGAM51 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM51 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM51 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM51 are further described hereinbelow with reference to Table 1.
- [0679] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM51 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0680] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 52 (VGAM52) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [0681] VGAM52 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM52 was detected is described hereinabove with reference to Figs. 2-8.

[0682] VGAM52 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0683] VGAM52 gene, herein designated VGAM GENE, encodes a VGAM52 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM52 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM52 precursor RNA is designated SEQ ID:710, and is provided hereinbelow with reference to the sequence listing part.

[0684] VGAM52 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM52 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[0685] An enzyme complex designated DICER COMPLEX, dices the VGAM52 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM52 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM52 RNA is designated SEQ ID:711, and is provided hereinbelow with reference to the sequence listing part.

[0686] VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0687] VGAM52 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM52 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM52 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0688] The complementary binding of VGAM52 RNA, herein designated VGAM RNA, to host target binding sites on VGAM52 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM52 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0689] It is appreciated that VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM52 host target genes. The mRNA of each one of this plurality of VGAM52 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM52 RNA, herein designated VGAM RNA, and which when bound by VGAM52 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM52 host target proteins.

[0690] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM52 gene, herein designated VGAM GENE, on one or more VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0691] It is yet further appreciated that a function of VGAM52 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM52 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM52 correlate with, and may be deduced from, the identity of the host target genes which VGAM52 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0692] Nucleotide sequences of the VGAM52 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM52 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM52 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM52 are further described hereinbelow with reference to Table 1.

[0693] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM52 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0694] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 53 (VGAM53) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0695] VGAM53 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM53 was detected is described hereinabove with reference to Figs. 2-8.

[0696] VGAM53 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human

genome.

[0697] VGAM53 gene, herein designated VGAM GENE, encodes a VGAM53 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM53 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM53 precursor RNA is designated SEQ ID:726, and is provided hereinbelow with reference to the sequence listing part.

[0698] VGAM53 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM53 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0699] An enzyme complex designated DICER COMPLEX, dices the VGAM53 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM53 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM53 RNA is designated SEQ ID:727, and is provided hereinbelow with reference to the sequence listing part.

[0700] VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0701] VGAM53 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide

sequence of VGAM53 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM53 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0702] The complementary binding of VGAM53 RNA, herein designated VGAM RNA, to host target binding sites on VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM53 host target protein, herein designated VGAM

HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0703] It is appreciated that VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM53 host target genes. The mRNA of each one of this plurality of VGAM53 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM53 RNA, herein designated VGAM RNA, and which when bound by VGAM53 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM53 host target proteins.

[0704] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM53 gene, herein designated VGAM GENE, on one or more VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also



believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0705] It is yet further appreciated that a function of VGAM53 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM53 correlate with, and may be deduced from, the identity of the host target genes which VGAM53 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0706] Nucleotide sequences of the VGAM53 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM53 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM53 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM53 are further described hereinbelow with reference to Table 1.

[0707] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM53 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0708] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 54 (VGAM54) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0709] VGAM54 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM54 was detected is described hereinabove with reference to Figs. 2-8.

[0710] VGAM54 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0711] VGAM54 gene, herein designated VGAM GENE, encodes a VGAM54 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM54 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM54 precursor RNA is designated SEQ ID:817, and is provided hereinbelow with reference to the sequence listing part.

[0712] VGAM54 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM54 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0713] An enzyme complex designated DICER COMPLEX, dices the VGAM54 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM54 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM54 RNA is designated SEQ ID:818, and is provided hereinbelow with reference to the sequence listing part.

[0714] VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0715] VGAM54 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM54 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target

binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM54 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0716] The complementary binding of VGAM54 RNA, herein designated VGAM RNA, to host target binding sites on VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM54 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0717] It is appreciated that VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM54 host target genes. The mRNA of each one of this plurality of VGAM54 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM54 RNA, herein designated VGAM RNA, and which when bound by VGAM54 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM54 host target proteins.

[0718] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM54 gene, herein designated VGAM GENE, on one or more VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective:

Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0719] It is yet further appreciated that a function of VGAM54 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM54 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM54 correlate with, and may be deduced from, the identity of the host target genes which VGAM54 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0720] Nucleotide sequences of the VGAM54 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM54 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM54 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM54 are further described hereinbelow with reference to Table 1.

[0721] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM54 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[0722] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 55 (VGAM55) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0723] VGAM55 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM55 was detected is described hereinabove with reference to Figs. 2–8.

[0724] VGAM55 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0725] VGAM55 gene, herein designated VGAM GENE, encodes a VGAM55 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM55 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM55 precursor RNA is



designated SEQ ID:830, and is provided hereinbelow with reference to the sequence listing part.

[0726] VGAM55 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM55 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0727] An enzyme complex designated DICER COMPLEX, dices the VGAM55 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM55 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM55 RNA is designated SEQ ID:831, and is provided hereinbelow with reference to the sequence list-

ing part.

[0728] VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0729] VGAM55 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing VGAM55 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0730] The complementary binding of VGAM55 RNA, herein designated VGAM RNA, to host target binding sites on VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM55 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0731] It is appreciated that VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM55 host target genes. The mRNA of each one of this plurality of VGAM55 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM55 RNA, herein designated VGAM RNA, and which when bound by VGAM55 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM55 host target proteins.

[0732] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM55 gene, herein designated VGAM GENE, on one or more VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0733] It is yet further appreciated that a function of VGAM55 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM55 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM55 correlate with, and may be deduced from, the identity of the host target genes which VGAM55 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [0734] Nucleotide sequences of the VGAM55 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM55 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM55 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM55 are further described hereinbelow with reference to Table 1.
- [0735] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM55 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0736] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 56 (VGAM56) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0737] VGAM56 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM56 was detected is described hereinabove with reference to Figs. 2–8.

[0738] VGAM56 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0739] VGAM56 gene, herein designated VGAM GENE, encodes a VGAM56 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM56 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM56 precursor RNA is designated SEQ ID:841, and is provided hereinbelow with reference to the sequence listing part.

[0740] VGAM56 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM56 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0741] An enzyme complex designated DICER COMPLEX, dices the VGAM56 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM56 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM56 RNA is designated SEQ ID:842, and is provided hereinbelow with reference to the sequence listing part.

[0742] VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM56 host target RNA, herein designated VGAM HOST

TARGET RNA. VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0743] VGAM56 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM56 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM56 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appre-



ciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0744] The complementary binding of VGAM56 RNA, herein designated VGAM RNA, to host target binding sites on VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM56 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0745] It is appreciated that VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM56 host target genes. The mRNA of each one of this plurality of VGAM56 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM56 RNA, herein designated VGAM RNA, and which when bound by VGAM56 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM56 host target proteins.

[0746] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM56 gene, herein designated VGAM GENE, on one or more VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0747] It is yet further appreciated that a function of VGAM56 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM56 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM56 correlate with, and may be deduced from, the identity of

the host target genes which VGAM56 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0748] Nucleotide sequences of the VGAM56 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM56 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM56 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM56 are further described hereinbelow with reference to Table 1.

[0749] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM56 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0750] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 57 (VGAM57) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0751] VGAM57 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM57 was detected is described hereinabove with reference to Figs. 2–8.

[0752] VGAM57 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0753] VGAM57 gene, herein designated VGAM GENE, encodes a VGAM57 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM57 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM57 precursor RNA is designated SEQ ID:860, and is provided hereinbelow with reference to the sequence listing part.

[0754] VGAM57 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM57 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0755] An enzyme complex designated DICER COMPLEX, dices the VGAM57 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM57 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM57 RNA is designated SEQ ID:861, and is provided hereinbelow with reference to the sequence listing part.

[0756] VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated

region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0757] VGAM57 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM57 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0758] The complementary binding of VGAM57 RNA, herein designated VGAM RNA, to host target binding sites on VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM57 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0759] It is appreciated that VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM57 host target genes. The mRNA of each one of this plurality of VGAM57 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM57 RNA, herein designated VGAM RNA, and which when bound by VGAM57 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM57 host target proteins.

[0760] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM57 gene, herein designated VGAM GENE, on one or

more VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0761] It is yet further appreciated that a function of VGAM57 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM57 correlate with, and may be deduced from, the identity of the host target genes which VGAM57 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0762] Nucleotide sequences of the VGAM57 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM57 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM57 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM57 are further described hereinbelow with reference to Table 1.

[0763] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM57 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0764] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 58 (VGAM58) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0765] VGAM58 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM58 was detected is described hereinabove with reference to Figs. 2-8.

[0766] VGAM58 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Porcine adenovirus A. VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0767] VGAM58 gene, herein designated VGAM GENE, encodes a VGAM58 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM58 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM58 precursor RNA is designated SEQ ID:879, and is provided hereinbelow with reference to the sequence listing part.

[0768] VGAM58 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM58 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0769] An enzyme complex designated DICER COMPLEX, dices the VGAM58 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM58 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM58 RNA is designated SEQ ID:880, and is provided hereinbelow with reference to the sequence listing part.

[0770] VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0771] VGAM58 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM58 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM58 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0772] The complementary binding of VGAM58 RNA, herein designated VGAM RNA, to host target binding sites on VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM58 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0773] It is appreciated that VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM58 host target genes. The mRNA of each one of this plurality of VGAM58 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM58 RNA, herein designated VGAM RNA, and which when bound by VGAM58 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM58 host target proteins.

[0774] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM58 gene, herein designated VGAM GENE, on one or more VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0775] It is yet further appreciated that a function of VGAM58 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM58 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM58 correlate with, and may be deduced from, the identity of the host target genes which VGAM58 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0776] Nucleotide sequences of the VGAM58 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM58 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM58 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM58 are further described hereinbelow with reference to Table 1.

[0777] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM58 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0778] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 59 (VGAM59) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0779] VGAM59 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM59 was detected is described hereinabove with reference to Figs. 2-8.

[0780] VGAM59 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0781] VGAM59 gene, herein designated VGAM GENE, encodes a VGAM59 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM59 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM59 precursor RNA is designated SEQ ID:899, and is provided hereinbelow with reference to the sequence listing part.

[0782] VGAM59 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM59 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0783] An enzyme complex designated DICER COMPLEX, dices the VGAM59 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM59 RNA, herein designated VGAM RNA, a single stranded ~22 nt



long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM59 RNA is designated SEQ ID:900, and is provided hereinbelow with reference to the sequence listing part.

[0784] VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0785] VGAM59 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM59 RNA, herein designated VGAM RNA,

is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM59 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0786] The complementary binding of VGAM59 RNA, herein designated VGAM RNA, to host target binding sites on VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM59 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is

therefore outlined by a broken line.

[0787] It is appreciated that VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM59 host target genes. The mRNA of each one of this plurality of VGAM59 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM59 RNA, herein designated VGAM RNA, and which when bound by VGAM59 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM59 host target proteins.

[0788] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM59 gene, herein designated VGAM GENE, on one or more VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression

of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0789] It is yet further appreciated that a function of VGAM59 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM59 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM59 correlate with, and may be deduced from, the identity of the host target genes which VGAM59 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0790] Nucleotide sequences of the VGAM59 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM59 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM59 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM59 are further described hereinbelow with reference to Table 1.

[0791] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM59 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0792] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 60 (VGAM60) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0793] VGAM60 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM60 was detected is described hereinabove with reference to Figs. 2–8.

[0794] VGAM60 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM60 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0795] VGAM60 gene, herein designated VGAM GENE, encodes a VGAM60 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM60 precursor RNA, herein des-

ignated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM60 precursor RNA is designated SEQ ID:914, and is provided hereinbelow with reference to the sequence listing part.

[0796] VGAM60 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM60 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0797] An enzyme complex designated DICER COMPLEX, dices the VGAM60 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM60 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM60 RNA is designated SEQ ID:915, and is provided hereinbelow with reference to the sequence listing part.

[0798] VGAM60 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0799] VGAM60 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II

and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM60 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0800] The complementary binding of VGAM60 RNA, herein designated VGAM RNA, to host target binding sites on VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM60 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0801] It is appreciated that VGAM60 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM60 host target genes. The mRNA of



each one of this plurality of VGAM60 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM60 RNA, herein designated VGAM RNA, and which when bound by VGAM60 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM60 host target proteins.

[0802] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM60 gene, herein designated VGAM GENE, on one or more VGAM60 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0803] It is yet further appreciated that a function of VGAM60 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM60 correlate with, and may be deduced from, the identity of the host target genes which VGAM60 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0804] Nucleotide sequences of the VGAM60 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM60 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM60 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM60 are further described hereinbelow with reference to Table 1.

[0805] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM60 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0806] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 61 (VGAM61) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0807] VGAM61 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM61 was detected is described hereinabove with reference to Figs. 2–8.

[0808] VGAM61 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0809] VGAM61 gene, herein designated VGAM GENE, encodes a VGAM61 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM61 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM61 precursor RNA is designated SEQ ID:920, and is provided hereinbelow with

reference to the sequence listing part.

[0810] VGAM61 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM61 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0811] An enzyme complex designated DICER COMPLEX, dices the VGAM61 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM61 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM61 RNA is designated SEQ ID:921, and is provided hereinbelow with reference to the sequence listing part.

[0812] VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0813] VGAM61 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM61 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0814] The complementary binding of VGAM61 RNA, herein designated VGAM RNA, to host target binding sites on VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM61 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0815] It is appreciated that VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM61 host target genes. The mRNA of each one of this plurality of VGAM61 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM61 RNA, herein designated VGAM

RNA, and which when bound by VGAM61 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM61 host target proteins.

[0816] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM61 gene, herein designated VGAM GENE, on one or more VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0817] It is yet further appreciated that a function of VGAM61 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM61 include diagnosis, prevention and

treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM61 correlate with, and may be deduced from, the identity of the host target genes which VGAM61 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [0818] Nucleotide sequences of the VGAM61 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM61 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM61 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM61 are further described hereinbelow with reference to Table 1.
- [0819] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM61 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0820] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 62 (VGAM62) viral gene, which modulates expres-



sion of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0821] VGAM62 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM62 was detected is described hereinabove with reference to Figs. 2–8.

[0822] VGAM62 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0823] VGAM62 gene, herein designated VGAM GENE, encodes a VGAM62 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM62 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM62 precursor RNA is designated SEQ ID:956, and is provided hereinbelow with reference to the sequence listing part.

[0824] VGAM62 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM62 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0825] An enzyme complex designated DICER COMPLEX, dices the VGAM62 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM62 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM62 RNA is designated SEQ ID:957, and is provided hereinbelow with reference to the sequence listing part.

[0826] VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM62 host target RNA, herein designated

VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0827] VGAM62 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM62 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in

the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0828] The complementary binding of VGAM62 RNA, herein designated VGAM RNA, to host target binding sites on VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM62 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0829] It is appreciated that VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM62 host target genes. The mRNA of each one of this plurality of VGAM62 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM62 RNA, herein designated VGAM RNA, and which when bound by VGAM62 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM62 host target proteins.

[0830] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM62 gene, herein designated VGAM GENE, on one or more VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0831] It is yet further appreciated that a function of VGAM62 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM62 correlate with, and may be deduced from, the identity of the host target genes which VGAM62 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[0832] Nucleotide sequences of the VGAM62 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM62 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM62 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM62 are further described hereinbelow with reference to Table 1.

[0833] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM62 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0834] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 63 (VGAM63) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0835] VGAM63 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM63 was detected is described hereinabove with reference to Figs. 2–8.

[0836] VGAM63 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM63 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0837] VGAM63 gene, herein designated VGAM GENE, encodes a VGAM63 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM63 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM63 precursor RNA is designated SEQ ID:1091, and is provided hereinbelow with reference to the sequence listing part.

[0838] VGAM63 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM63 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0839] An enzyme complex designated DICER COMPLEX, dices the VGAM63 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM63 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM63 RNA is designated SEQ ID:1092, and is provided hereinbelow with reference to the sequence listing part.

[0840] VGAM63 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR re-



spectively.

[0841] VGAM63 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM63 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM63 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0842] The complementary binding of VGAM63 RNA, herein des-

ignated VGAM RNA, to host target binding sites on VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM63 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0843] It is appreciated that VGAM63 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM63 host target genes. The mRNA of each one of this plurality of VGAM63 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM63 RNA, herein designated VGAM RNA, and which when bound by VGAM63 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM63 host target proteins.

[0844] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM63 gene, herein designated VGAM GENE, on one or more VGAM63 host target gene, herein designated VGAM

HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0845] It is yet further appreciated that a function of VGAM63 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM63 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM63 correlate with, and may be deduced from, the identity of the host target genes which VGAM63 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0846] Nucleotide sequences of the VGAM63 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM63 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM63 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM63 are further described hereinbelow with reference to Table 1.

[0847] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM63 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0848] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 64 (VGAM64) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0849] VGAM64 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM64 was detected is described hereinabove with reference to Figs. 2-8.

[0850] VGAM64 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A.

VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0851] VGAM64 gene, herein designated VGAM GENE, encodes a VGAM64 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM64 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM64 precursor RNA is designated SEQ ID:1108, and is provided hereinbelow with reference to the sequence listing part.

[0852] VGAM64 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM64 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0853] An enzyme complex designated DICER COMPLEX, dices

the VGAM64 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM64 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM64 RNA is designated SEQ ID:1109, and is provided hereinbelow with reference to the sequence listing part.

[0854] VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0855] VGAM64 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM64 host target RNA,

herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM64 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0856] The complementary binding of VGAM64 RNA, herein designated VGAM RNA, to host target binding sites on VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM64 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM64 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0857] It is appreciated that VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM64 host target genes. The mRNA of each one of this plurality of VGAM64 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM64 RNA, herein designated VGAM RNA, and which when bound by VGAM64 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM64 host target proteins.

[0858] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM64 gene, herein designated VGAM GENE, on one or more VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only



for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0859] It is yet further appreciated that a function of VGAM64 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM64 correlate with, and may be deduced from, the identity of the host target genes which VGAM64 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0860] Nucleotide sequences of the VGAM64 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM64 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM64 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM64 are further de-

scribed hereinbelow with reference to Table 1.

[0861] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM64 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0862] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 65 (VGAM65) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0863] VGAM65 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM65 was detected is described hereinabove with reference to Figs. 2-8.

[0864] VGAM65 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM65 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0865] VGAM65 gene, herein designated VGAM GENE, encodes a

VGAM65 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM65 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM65 precursor RNA is designated SEQ ID:1119, and is provided hereinbelow with reference to the sequence listing part.

[0866] VGAM65 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM65 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0867] An enzyme complex designated DICER COMPLEX, dices the VGAM65 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM65 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM65 RNA is designated SEQ ID:1120, and is provided hereinbelow with reference to the sequence listing part.

[0868] VGAM65 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0869] VGAM65 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of

the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM65 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0870] The complementary binding of VGAM65 RNA, herein designated VGAM RNA, to host target binding sites on VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM65 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0871] It is appreciated that VGAM65 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM65 host target genes. The mRNA of each one of this plurality of VGAM65 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM65 RNA, herein designated VGAM RNA, and which when bound by VGAM65 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM65 host target proteins.

[0872] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM65 gene, herein designated VGAM GENE, on one or more VGAM65 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although spe-

cific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0873] It is yet further appreciated that a function of VGAM65 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM65 correlate with, and may be deduced from, the identity of the host target genes which VGAM65 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0874] Nucleotide sequences of the VGAM65 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM65 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM65 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM65 are further described hereinbelow with reference to Table 1.

[0875] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM65 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0876] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 66 (VGAM66) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0877] VGAM66 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM66 was detected is described hereinabove with reference to Figs. 2–8.

[0878] VGAM66 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM66 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0879] VGAM66 gene, herein designated VGAM GENE, encodes a VGAM66 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM66 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a pro-



tein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM66 precursor RNA is designated SEQ ID:1166, and is provided hereinbelow with reference to the sequence listing part.

[0880] VGAM66 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM66 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0881] An enzyme complex designated DICER COMPLEX, dices the VGAM66 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM66 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM66 RNA is designated SEQ ID:1167, and is provided hereinbelow with reference to the sequence listing part.

[0882] VGAM66 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0883] VGAM66 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM66 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0884] The complementary binding of VGAM66 RNA, herein designated VGAM RNA, to host target binding sites on VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM66 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0885] It is appreciated that VGAM66 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM66 host target genes. The mRNA of each one of this plurality of VGAM66 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM66 RNA, herein designated VGAM RNA, and which when bound by VGAM66 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM66 host target proteins.

[0886] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM66 gene, herein designated VGAM GENE, on one or more VGAM66 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0887] It is yet further appreciated that a function of VGAM66 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM66 correlate with, and may be deduced from, the identity of the host target genes which VGAM66 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0888] Nucleotide sequences of the VGAM66 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM66 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM66 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM66 are further described hereinbelow with reference to Table 1.

[0889] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM66 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0890] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 67 (VGAM67) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0891] VGAM67 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM67 was detected is described hereinabove with reference to Figs. 2–8.

[0892] VGAM67 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus. VGAM67 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0893] VGAM67 gene, herein designated VGAM GENE, encodes a VGAM67 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM67 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM67 precursor RNA is designated SEQ ID:1184, and is provided hereinbelow with reference to the sequence listing part.

[0894] VGAM67 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM67 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0895] An enzyme complex designated DICER COMPLEX, dices the VGAM67 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM67 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM67 RNA is designated SEQ ID:1185, and is provided hereinbelow with reference to the sequence listing part.

[0896] VGAM67 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA,

VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0897] VGAM67 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM67 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM67 host target RNA, herein



designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0898] The complementary binding of VGAM67 RNA, herein designated VGAM RNA, to host target binding sites on VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM67 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0899] It is appreciated that VGAM67 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM67 host target genes. The mRNA of each one of this plurality of VGAM67 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM67 RNA, herein designated VGAM RNA, and which when bound by VGAM67 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM67 host target proteins.

[0900] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM67 gene, herein designated VGAM GENE, on one or more VGAM67 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0901] It is yet further appreciated that a function of VGAM67 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM67 correlate

with, and may be deduced from, the identity of the host target genes which VGAM67 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0902] Nucleotide sequences of the VGAM67 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM67 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM67 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM67 are further described hereinbelow with reference to Table 1.

[0903] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM67 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0904] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 68 (VGAM68) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

- [0905] VGAM68 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM68 was detected is described hereinabove with reference to Figs. 2–8.
- [0906] VGAM68 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM68 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [0907] VGAM68 gene, herein designated VGAM GENE, encodes a VGAM68 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM68 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM68 precursor RNA is designated SEQ ID:1195, and is provided hereinbelow with reference to the sequence listing part.
- [0908] VGAM68 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM68 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0909] An enzyme complex designated DICER COMPLEX, dices the VGAM68 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM68 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM68 RNA is designated SEQ ID:1196, and is provided hereinbelow with reference to the sequence listing part.

[0910] VGAM68 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untrans-

lated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0911] VGAM68 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM68 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR re-

gion, the 5UTR region, or in both 3UTR and 5UTR regions.

[0912] The complementary binding of VGAM68 RNA, herein designated VGAM RNA, to host target binding sites on VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM68 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0913] It is appreciated that VGAM68 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM68 host target genes. The mRNA of each one of this plurality of VGAM68 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM68 RNA, herein designated VGAM RNA, and which when bound by VGAM68 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM68 host target proteins.

[0914] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM68 gene, herein designated VGAM GENE, on one or more VGAM68 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0915] It is yet further appreciated that a function of VGAM68 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM68 correlate with, and may be deduced from, the identity of the host target genes which VGAM68 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



- [0916] Nucleotide sequences of the VGAM68 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM68 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM68 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM68 are further described hereinbelow with reference to Table 1.
- [0917] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM68 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [0918] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 69 (VGAM69) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [0919] VGAM69 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM69 was detected is described hereinabove with reference to Figs. 2-8.

[0920] VGAM69 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0921] VGAM69 gene, herein designated VGAM GENE, encodes a VGAM69 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM69 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM69 precursor RNA is designated SEQ ID:1199, and is provided hereinbelow with reference to the sequence listing part.

[0922] VGAM69 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM69 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[0923] An enzyme complex designated DICER COMPLEX, dices the VGAM69 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM69 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM69 RNA is designated SEQ ID:1200, and is provided hereinbelow with reference to the sequence listing part.

[0924] VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0925] VGAM69 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM69 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM69 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0926] The complementary binding of VGAM69 RNA, herein designated VGAM RNA, to host target binding sites on VGAM69 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM69 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0927] It is appreciated that VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM69 host target genes. The mRNA of each one of this plurality of VGAM69 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM69 RNA, herein designated VGAM RNA, and which when bound by VGAM69 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM69 host target proteins.

[0928] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM69 gene, herein designated VGAM GENE, on one or more VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0929] It is yet further appreciated that a function of VGAM69 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM69 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM69 correlate with, and may be deduced from, the identity of the host target genes which VGAM69 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0930] Nucleotide sequences of the VGAM69 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM69 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM69 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM69 are further described hereinbelow with reference to Table 1.

[0931] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM69 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0932] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 70 (VGAM70) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0933] VGAM70 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM70 was detected is described hereinabove with reference to Figs. 2-8.

[0934] VGAM70 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human

genome.

[0935] VGAM70 gene, herein designated VGAM GENE, encodes a VGAM70 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM70 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM70 precursor RNA is designated SEQ ID:1205, and is provided hereinbelow with reference to the sequence listing part.

[0936] VGAM70 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM70 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0937] An enzyme complex designated DICER COMPLEX, dices the VGAM70 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM70 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM70 RNA is designated SEQ ID:1206, and is provided hereinbelow with reference to the sequence listing part.

[0938] VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0939] VGAM70 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide

sequence of VGAM70 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM70 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0940] The complementary binding of VGAM70 RNA, herein designated VGAM RNA, to host target binding sites on VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM70 host target protein, herein designated VGAM

HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0941] It is appreciated that VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM70 host target genes. The mRNA of each one of this plurality of VGAM70 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM70 RNA, herein designated VGAM RNA, and which when bound by VGAM70 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM70 host target proteins.

[0942] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM70 gene, herein designated VGAM GENE, on one or more VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0943] It is yet further appreciated that a function of VGAM70 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM70 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM70 correlate with, and may be deduced from, the identity of the host target genes which VGAM70 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0944] Nucleotide sequences of the VGAM70 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM70 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM70 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM70 are further described hereinbelow with reference to Table 1.

[0945] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM70 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0946] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 71 (VGAM71) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0947] VGAM71 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM71 was detected is described hereinabove with reference to Figs. 2-8.

[0948] VGAM71 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0949] VGAM71 gene, herein designated VGAM GENE, encodes a VGAM71 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM71 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM71 precursor RNA is designated SEQ ID:1233, and is provided hereinbelow with reference to the sequence listing part.

[0950] VGAM71 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM71 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0951] An enzyme complex designated DICER COMPLEX, dices the VGAM71 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM71 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM71 RNA is designated SEQ ID:1234, and is provided hereinbelow with reference to the sequence listing part.

[0952] VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0953] VGAM71 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target

binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM71 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0954] The complementary binding of VGAM71 RNA, herein designated VGAM RNA, to host target binding sites on VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM71 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0955] It is appreciated that VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM71 host target genes. The mRNA of each one of this plurality of VGAM71 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM71 RNA, herein designated VGAM RNA, and which when bound by VGAM71 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM71 host target proteins.

[0956] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM71 gene, herein designated VGAM GENE, on one or more VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective:

Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0957] It is yet further appreciated that a function of VGAM71 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM71 correlate with, and may be deduced from, the identity of the host target genes which VGAM71 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0958] Nucleotide sequences of the VGAM71 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM71 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM71 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM71 are further described hereinbelow with reference to Table 1.

[0959] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM71 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[0960] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 72 (VGAM72) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0961] VGAM72 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM72 was detected is described hereinabove with reference to Figs. 2–8.

[0962] VGAM72 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0963] VGAM72 gene, herein designated VGAM GENE, encodes a VGAM72 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM72 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM72 precursor RNA is

designated SEQ ID:1238, and is provided hereinbelow with reference to the sequence listing part.

[0964] VGAM72 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM72 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0965] An enzyme complex designated DICER COMPLEX, dices the VGAM72 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM72 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM72 RNA is designated SEQ ID:1239, and is provided hereinbelow with reference to the sequence list-

ing part.

[0966] VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0967] VGAM72 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing VGAM72 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0968] The complementary binding of VGAM72 RNA, herein designated VGAM RNA, to host target binding sites on VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM72 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0969] It is appreciated that VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM72 host target genes. The mRNA of each one of this plurality of VGAM72 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM72 RNA, herein designated VGAM RNA, and which when bound by VGAM72 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM72 host target proteins.

[0970] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM72 gene, herein designated VGAM GENE, on one or more VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0971] It is yet further appreciated that a function of VGAM72 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM72 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM72 correlate with, and may be deduced from, the identity of the host target genes which VGAM72 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0972] Nucleotide sequences of the VGAM72 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM72 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM72 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM72 are further described hereinbelow with reference to Table 1.

[0973] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM72 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0974] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 73 (VGAM73) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0975] VGAM73 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM73 was detected is described hereinabove with reference to Figs. 2–8.

[0976] VGAM73 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian T-lymphotropic virus 2. VGAM73 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0977] VGAM73 gene, herein designated VGAM GENE, encodes a VGAM73 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM73 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM73 precursor RNA is designated SEQ ID:1260, and is provided hereinbelow with reference to the sequence listing part.

[0978] VGAM73 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM73 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0979] An enzyme complex designated DICER COMPLEX, dices the VGAM73 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM73 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM73 RNA is designated SEQ ID:1261, and is provided hereinbelow with reference to the sequence listing part.

[0980] VGAM73 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM73 host target RNA, herein designated VGAM HOST

TARGET RNA. VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0981] VGAM73 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM73 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM73 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appre-

ciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0982] The complementary binding of VGAM73 RNA, herein designated VGAM RNA, to host target binding sites on VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM73 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0983] It is appreciated that VGAM73 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM73 host target genes. The mRNA of each one of this plurality of VGAM73 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM73 RNA, herein designated VGAM RNA, and which when bound by VGAM73 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM73 host target proteins.

[0984] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM73 gene, herein designated VGAM GENE, on one or more VGAM73 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0985] It is yet further appreciated that a function of VGAM73 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM73 include diagnosis, prevention and treatment of viral infection by Simian T-lymphotropic virus 2. Specific functions, and accordingly utilities, of VGAM73 correlate with, and may be deduced from, the

identity of the host target genes which VGAM73 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[0986] Nucleotide sequences of the VGAM73 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM73 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM73 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM73 are further described hereinbelow with reference to Table 1.

[0987] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM73 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[0988] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 74 (VGAM74) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[0989] VGAM74 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM74 was detected is described hereinabove with reference to Figs. 2–8.

[0990] VGAM74 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[0991] VGAM74 gene, herein designated VGAM GENE, encodes a VGAM74 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM74 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM74 precursor RNA is designated SEQ ID:1289, and is provided hereinbelow with reference to the sequence listing part.

[0992] VGAM74 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM74 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[0993] An enzyme complex designated DICER COMPLEX, dices the VGAM74 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM74 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM74 RNA is designated SEQ ID:1290, and is provided hereinbelow with reference to the sequence listing part.

[0994] VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated



region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[0995] VGAM74 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM74 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[0996] The complementary binding of VGAM74 RNA, herein designated VGAM RNA, to host target binding sites on VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM74 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[0997] It is appreciated that VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM74 host target genes. The mRNA of each one of this plurality of VGAM74 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM74 RNA, herein designated VGAM RNA, and which when bound by VGAM74 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM74 host target proteins.

[0998] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM74 gene, herein designated VGAM GENE, on one or

more VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[0999] It is yet further appreciated that a function of VGAM74 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM74 correlate with, and may be deduced from, the identity of the host target genes which VGAM74 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1000] Nucleotide sequences of the VGAM74 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM74 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM74 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM74 are further described hereinbelow with reference to Table 1.

[1001] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM74 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1002] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 75 (VGAM75) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1003] VGAM75 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM75 was detected is described hereinabove with reference to Figs. 2-8.

[1004] VGAM75 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Simian T-lymphotropic virus 2. VGAM75 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1005] VGAM75 gene, herein designated VGAM GENE, encodes a VGAM75 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM75 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM75 precursor RNA is designated SEQ ID:1304, and is provided hereinbelow with reference to the sequence listing part.

[1006] VGAM75 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM75 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1007] An enzyme complex designated DICER COMPLEX, dices the VGAM75 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM75 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM75 RNA is designated SEQ ID:1305, and is provided hereinbelow with reference to the sequence listing part.

[1008] VGAM75 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM75 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM75 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1009] VGAM75 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM75 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM75 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM75 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1010] The complementary binding of VGAM75 RNA, herein designated VGAM RNA, to host target binding sites on VGAM75 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM75 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM75 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1011] It is appreciated that VGAM75 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM75 host target genes. The mRNA of each one of this plurality of VGAM75 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM75 RNA, herein designated VGAM RNA, and which when bound by VGAM75 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM75 host target proteins.

[1012] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM75 gene, herein designated VGAM GENE, on one or more VGAM75 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific



complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1013] It is yet further appreciated that a function of VGAM75 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of viral infection by Simian T-lymphotropic virus 2. Specific functions, and accordingly utilities, of VGAM75 correlate with, and may be deduced from, the identity of the host target genes which VGAM75 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1014] Nucleotide sequences of the VGAM75 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM75 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM75 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM75 are further described hereinbelow with reference to Table 1.

[1015] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM75 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1016] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 76 (VGAM76) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1017] VGAM76 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM76 was detected is described hereinabove with reference to Figs. 2-8.

[1018] VGAM76 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1019] VGAM76 gene, herein designated VGAM GENE, encodes a VGAM76 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM76 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM76 precursor RNA is designated SEQ ID:1349, and is provided hereinbelow with reference to the sequence listing part.

[1020] VGAM76 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM76 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1021] An enzyme complex designated DICER COMPLEX, dices the VGAM76 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM76 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM76 RNA is designated SEQ ID:1350, and is provided hereinbelow with reference to the sequence listing part.

[1022] VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1023] VGAM76 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA,

is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM76 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1024] The complementary binding of VGAM76 RNA, herein designated VGAM RNA, to host target binding sites on VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM76 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is

therefore outlined by a broken line.

[1025] It is appreciated that VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM76 host target genes. The mRNA of each one of this plurality of VGAM76 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM76 RNA, herein designated VGAM RNA, and which when bound by VGAM76 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM76 host target proteins.

[1026] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM76 gene, herein designated VGAM GENE, on one or more VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression

of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1027] It is yet further appreciated that a function of VGAM76 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM76 correlate with, and may be deduced from, the identity of the host target genes which VGAM76 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1028] Nucleotide sequences of the VGAM76 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM76 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM76 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM76 are further described hereinbelow with reference to Table 1.

[1029] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM76 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1030] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 77 (VGAM77) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1031] VGAM77 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM77 was detected is described hereinabove with reference to Figs. 2–8.

[1032] VGAM77 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1033] VGAM77 gene, herein designated VGAM GENE, encodes a VGAM77 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM77 precursor RNA, herein des-



ignated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM77 precursor RNA is designated SEQ ID:1434, and is provided hereinbelow with reference to the sequence listing part.

[1034] VGAM77 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM77 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1035] An enzyme complex designated DICER COMPLEX, dices the VGAM77 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM77 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM77 RNA is designated SEQ ID:1435, and is provided hereinbelow with reference to the sequence listing part.

[1036] VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1037] VGAM77 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM77 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II

and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM77 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1038] The complementary binding of VGAM77 RNA, herein designated VGAM RNA, to host target binding sites on VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM77 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1039] It is appreciated that VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM77 host target genes. The mRNA of each one of this plurality of VGAM77 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM77 RNA, herein designated VGAM RNA, and which when bound by VGAM77 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM77 host target proteins.

[1040] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM77 gene, herein designated VGAM GENE, on one or

more VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1041] It is yet further appreciated that a function of VGAM77 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM77 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM77 correlate with, and may be deduced from, the identity of the host target genes which VGAM77 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1042] Nucleotide sequences of the VGAM77 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM77 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM77 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM77 are further described hereinbelow with reference to Table 1.

[1043] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM77 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1044] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 78 (VGAM78) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1045] VGAM78 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM78 was detected is described hereinabove with reference to Figs. 2-8.

[1046] VGAM78 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Rat cytomegalovirus.

VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1047] VGAM78 gene, herein designated VGAM GENE, encodes a VGAM78 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM78 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM78 precursor RNA is designated SEQ ID:1446, and is provided hereinbelow with reference to the sequence listing part.

[1048] VGAM78 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM78 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1049] An enzyme complex designated DICER COMPLEX, dices the VGAM78 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM78 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM78 RNA is designated SEQ ID:1447, and is provided hereinbelow with reference to the sequence listing part.

[1050] VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1051] VGAM78 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM78 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM78 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1052] The complementary binding of VGAM78 RNA, herein designated VGAM RNA, to host target binding sites on VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM78 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1053] It is appreciated that VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM78 host target genes. The mRNA of each one of this plurality of VGAM78 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM78 RNA, herein designated VGAM RNA, and which when bound by VGAM78 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM78 host target proteins.

[1054] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM78 gene, herein designated VGAM GENE, on one or more VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1055] It is yet further appreciated that a function of VGAM78 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM78 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM78 correlate with, and may be deduced from, the identity of the host target genes which VGAM78 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1056] Nucleotide sequences of the VGAM78 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM78 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM78 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM78 are further described hereinbelow with reference to Table 1.

[1057] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM78 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1058] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 79 (VGAM79) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1059] VGAM79 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM79 was detected is described hereinabove with reference to Figs. 2-8.

[1060] VGAM79 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1061] VGAM79 gene, herein designated VGAM GENE, encodes a VGAM79 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM79 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM79 precursor RNA is designated SEQ ID:1450, and is provided hereinbelow with reference to the sequence listing part.

[1062] VGAM79 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM79 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1063] An enzyme complex designated DICER COMPLEX, dices the VGAM79 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM79 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM79 RNA is designated SEQ ID:1451, and is provided hereinbelow with reference to the sequence listing part.

[1064] VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1065] VGAM79 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM79 RNA, herein designated VGAM RNA,

is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM79 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1066] The complementary binding of VGAM79 RNA, herein designated VGAM RNA, to host target binding sites on VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM79 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is

therefore outlined by a broken line.

[1067] It is appreciated that VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM79 host target genes. The mRNA of each one of this plurality of VGAM79 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM79 RNA, herein designated VGAM RNA, and which when bound by VGAM79 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM79 host target proteins.

[1068] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM79 gene, herein designated VGAM GENE, on one or more VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression



of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1069] It is yet further appreciated that a function of VGAM79 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM79 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM79 correlate with, and may be deduced from, the identity of the host target genes which VGAM79 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1070] Nucleotide sequences of the VGAM79 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM79 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM79 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM79 are further described hereinbelow with reference to Table 1.

[1071] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM79 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1072] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 80 (VGAM80) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1073] VGAM80 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM80 was detected is described hereinabove with reference to Figs. 2–8.

[1074] VGAM80 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1075] VGAM80 gene, herein designated VGAM GENE, encodes a VGAM80 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM80 precursor RNA, herein des-

ignated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM80 precursor RNA is designated SEQ ID:1481, and is provided hereinbelow with reference to the sequence listing part.

[1076] VGAM80 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM80 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1077] An enzyme complex designated DICER COMPLEX, dices the VGAM80 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM80 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 75%) nucleotide sequence of VGAM80 RNA is designated SEQ ID:1482, and is provided hereinbelow with reference to the sequence listing part.

[1078] VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1079] VGAM80 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM80 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II

and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM80 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1080] The complementary binding of VGAM80 RNA, herein designated VGAM RNA, to host target binding sites on VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM80 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1081] It is appreciated that VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM80 host target genes. The mRNA of

each one of this plurality of VGAM80 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM80 RNA, herein designated VGAM RNA, and which when bound by VGAM80 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM80 host target proteins.

[1082] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM80 gene, herein designated VGAM GENE, on one or more VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1083] It is yet further appreciated that a function of VGAM80 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM80 correlate with, and may be deduced from, the identity of the host target genes which VGAM80 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1084] Nucleotide sequences of the VGAM80 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM80 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM80 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM80 are further described hereinbelow with reference to Table 1.

[1085] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM80 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1086] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 81 (VGAM81) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1087] VGAM81 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM81 was detected is described hereinabove with reference to Figs. 2–8.

[1088] VGAM81 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1089] VGAM81 gene, herein designated VGAM GENE, encodes a VGAM81 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM81 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM81 precursor RNA is designated SEQ ID:1564, and is provided hereinbelow with



reference to the sequence listing part.

[1090] VGAM81 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM81 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1091] An enzyme complex designated DICER COMPLEX, dices the VGAM81 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM81 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM81 RNA is designated SEQ ID:1565, and is provided hereinbelow with reference to the sequence listing part.

[1092] VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1093] VGAM81 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM81 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM81 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1094] The complementary binding of VGAM81 RNA, herein designated VGAM RNA, to host target binding sites on VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM81 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1095] It is appreciated that VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM81 host target genes. The mRNA of each one of this plurality of VGAM81 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM81 RNA, herein designated VGAM

RNA, and which when bound by VGAM81 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM81 host target proteins.

[1096] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM81 gene, herein designated VGAM GENE, on one or more VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1097] It is yet further appreciated that a function of VGAM81 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM81 include diagnosis, prevention and

treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM81 correlate with, and may be deduced from, the identity of the host target genes which VGAM81 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1098] Nucleotide sequences of the VGAM81 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM81 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM81 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM81 are further described hereinbelow with reference to Table 1.

[1099] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM81 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1100] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 82 (VGAM82) viral gene, which modulates expres-

sion of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1101] VGAM82 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM82 was detected is described hereinabove with reference to Figs. 2–8.

[1102] VGAM82 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1103] VGAM82 gene, herein designated VGAM GENE, encodes a VGAM82 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM82 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM82 precursor RNA is designated SEQ ID:1616, and is provided hereinbelow with reference to the sequence listing part.

[1104] VGAM82 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM82 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1105] An enzyme complex designated DICER COMPLEX, dices the VGAM82 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM82 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM82 RNA is designated SEQ ID:1617, and is provided hereinbelow with reference to the sequence listing part.

[1106] VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM82 host target RNA, herein designated

VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1107] VGAM82 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM82 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM82 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in



the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1108] The complementary binding of VGAM82 RNA, herein designated VGAM RNA, to host target binding sites on VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM82 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1109] It is appreciated that VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM82 host target genes. The mRNA of each one of this plurality of VGAM82 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM82 RNA, herein designated VGAM RNA, and which when bound by VGAM82 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM82 host target proteins.

[1110] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM82 gene, herein designated VGAM GENE, on one or more VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1111] It is yet further appreciated that a function of VGAM82 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM82 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM82 correlate with, and may be deduced from, the identity of the host target genes which VGAM82 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

- [1112] Nucleotide sequences of the VGAM82 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM82 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM82 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM82 are further described hereinbelow with reference to Table 1.
- [1113] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM82 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1114] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 83 (VGAM83) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [1115] VGAM83 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM83 was detected is described hereinabove with reference to Figs. 2–8.

[1116] VGAM83 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM83 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1117] VGAM83 gene, herein designated VGAM GENE, encodes a VGAM83 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM83 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM83 precursor RNA is designated SEQ ID:1623, and is provided hereinbelow with reference to the sequence listing part.

[1118] VGAM83 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM83 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1119] An enzyme complex designated DICER COMPLEX, dices the VGAM83 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM83 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM83 RNA is designated SEQ ID:1624, and is provided hereinbelow with reference to the sequence listing part.

[1120] VGAM83 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR re-

spectively.

[1121] VGAM83 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM83 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM83 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1122] The complementary binding of VGAM83 RNA, herein des-

ignated VGAM RNA, to host target binding sites on VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM83 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1123] It is appreciated that VGAM83 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM83 host target genes. The mRNA of each one of this plurality of VGAM83 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM83 RNA, herein designated VGAM RNA, and which when bound by VGAM83 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM83 host target proteins.

[1124] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM83 gene, herein designated VGAM GENE, on one or more VGAM83 host target gene, herein designated VGAM

HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1125] It is yet further appreciated that a function of VGAM83 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM83 correlate with, and may be deduced from, the identity of the host target genes which VGAM83 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1126] Nucleotide sequences of the VGAM83 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



diced VGAM83 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM83 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM83 are further described hereinbelow with reference to Table 1.

[1127] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM83 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1128] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 84 (VGAM84) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1129] VGAM84 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM84 was detected is described hereinabove with reference to Figs. 2-8.

[1130] VGAM84 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4.

VGAM84 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1131] VGAM84 gene, herein designated VGAM GENE, encodes a VGAM84 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM84 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM84 precursor RNA is designated SEQ ID:1628, and is provided hereinbelow with reference to the sequence listing part.

[1132] VGAM84 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM84 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1133] An enzyme complex designated DICER COMPLEX, dices

the VGAM84 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM84 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM84 RNA is designated SEQ ID:1629, and is provided hereinbelow with reference to the sequence listing part.

[1134] VGAM84 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1135] VGAM84 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM84 host target RNA,

herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM84 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM84 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1136] The complementary binding of VGAM84 RNA, herein designated VGAM RNA, to host target binding sites on VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM84 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM84 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1137] It is appreciated that VGAM84 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM84 host target genes. The mRNA of each one of this plurality of VGAM84 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM84 RNA, herein designated VGAM RNA, and which when bound by VGAM84 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM84 host target proteins.

[1138] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM84 gene, herein designated VGAM GENE, on one or more VGAM84 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only

for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1139] It is yet further appreciated that a function of VGAM84 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM84 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM84 correlate with, and may be deduced from, the identity of the host target genes which VGAM84 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1140] Nucleotide sequences of the VGAM84 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM84 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM84 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM84 are further de-

scribed hereinbelow with reference to Table 1.

[1141] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM84 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1142] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 85 (VGAM85) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1143] VGAM85 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM85 was detected is described hereinabove with reference to Figs. 2-8.

[1144] VGAM85 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1145] VGAM85 gene, herein designated VGAM GENE, encodes a

VGAM85 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM85 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM85 precursor RNA is designated SEQ ID:1774, and is provided hereinbelow with reference to the sequence listing part.

[1146] VGAM85 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM85 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1147] An enzyme complex designated DICER COMPLEX, dices the VGAM85 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM85 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM85 RNA is designated SEQ ID:1775, and is provided hereinbelow with reference to the sequence listing part.

[1148] VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1149] VGAM85 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of

the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM85 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1150] The complementary binding of VGAM85 RNA, herein designated VGAM RNA, to host target binding sites on VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM85 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1151] It is appreciated that VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM85 host target genes. The mRNA of each one of this plurality of VGAM85 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM85 RNA, herein designated VGAM RNA, and which when bound by VGAM85 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM85 host target proteins.

[1152] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM85 gene, herein designated VGAM GENE, on one or more VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although spe-

cific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1153] It is yet further appreciated that a function of VGAM85 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM85 correlate with, and may be deduced from, the identity of the host target genes which VGAM85 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1154] Nucleotide sequences of the VGAM85 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM85 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM85 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM85 are further described hereinbelow with reference to Table 1.

[1155] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM85 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1156] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 86 (VGAM86) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1157] VGAM86 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM86 was detected is described hereinabove with reference to Figs. 2–8.

[1158] VGAM86 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1159] VGAM86 gene, herein designated VGAM GENE, encodes a VGAM86 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM86 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a pro-

tein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM86 precursor RNA is designated SEQ ID:1816, and is provided hereinbelow with reference to the sequence listing part.

[1160] VGAM86 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM86 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1161] An enzyme complex designated DICER COMPLEX, dices the VGAM86 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM86 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM86 RNA is designated SEQ ID:1817, and is provided hereinbelow with reference to the sequence listing part.

[1162] VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1163] VGAM86 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM86 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM86 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1164] The complementary binding of VGAM86 RNA, herein designated VGAM RNA, to host target binding sites on VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM86 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1165] It is appreciated that VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM86 host target genes. The mRNA of each one of this plurality of VGAM86 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM86 RNA, herein designated VGAM RNA, and which when bound by VGAM86 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM86 host target proteins.

[1166] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM86 gene, herein designated VGAM GENE, on one or more VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1167] It is yet further appreciated that a function of VGAM86 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM86 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM86 correlate with, and may be deduced from, the identity of the host target genes which VGAM86 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1168] Nucleotide sequences of the VGAM86 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM86 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM86 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM86 are further described hereinbelow with reference to Table 1.

[1169] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM86 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1170] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 87 (VGAM87) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1171] VGAM87 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM87 was detected is described hereinabove with reference to Figs. 2–8.

[1172] VGAM87 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM87 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1173] VGAM87 gene, herein designated VGAM GENE, encodes a VGAM87 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM87 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM87 precursor RNA is designated SEQ ID:2007, and is provided hereinbelow with reference to the sequence listing part.

[1174] VGAM87 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM87 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1175] An enzyme complex designated DICER COMPLEX, dices the VGAM87 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM87 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM87 RNA is designated SEQ ID:2008, and is provided hereinbelow with reference to the sequence listing part.

[1176] VGAM87 host target gene, herein designated VGAM HOST

TARGET GENE, encodes a corresponding messenger RNA, VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1177] VGAM87 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM87 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1178] The complementary binding of VGAM87 RNA, herein designated VGAM RNA, to host target binding sites on VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM87 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1179] It is appreciated that VGAM87 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM87 host target genes. The mRNA of each one of this plurality of VGAM87 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM87 RNA, herein designated VGAM RNA, and which when bound by VGAM87 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM87 host target proteins.

[1180] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM87 gene, herein designated VGAM GENE, on one or more VGAM87 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1181] It is yet further appreciated that a function of VGAM87 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Spe-

cific functions, and accordingly utilities, of VGAM87 correlate with, and may be deduced from, the identity of the host target genes which VGAM87 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [1182] Nucleotide sequences of the VGAM87 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM87 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM87 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM87 are further described hereinbelow with reference to Table 1.
- [1183] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM87 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1184] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 88 (VGAM88) viral gene, which modulates expression of respective host target genes thereof, the function



and utility of which host target genes is known in the art.

[1185] VGAM88 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM88 was detected is described hereinabove with reference to Figs. 2–8.

[1186] VGAM88 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1187] VGAM88 gene, herein designated VGAM GENE, encodes a VGAM88 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM88 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM88 precursor RNA is designated SEQ ID:2036, and is provided hereinbelow with reference to the sequence listing part.

[1188] VGAM88 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM88 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1189] An enzyme complex designated DICER COMPLEX, dices the VGAM88 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM88 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM88 RNA is designated SEQ ID:2037, and is provided hereinbelow with reference to the sequence listing part.

[1190] VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is

typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1191] VGAM88 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM88 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM88 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these

host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1192] The complementary binding of VGAM88 RNA, herein designated VGAM RNA, to host target binding sites on VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM88 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1193] It is appreciated that VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM88 host target genes. The mRNA of each one of this plurality of VGAM88 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM88 RNA, herein designated VGAM RNA, and which when bound by VGAM88 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM88 host target proteins.

[1194] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM88 gene, herein designated VGAM GENE, on one or more VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1195] It is yet further appreciated that a function of VGAM88 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM88 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM88 correlate with, and may be deduced from, the identity of the host target genes which VGAM88 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [1196] Nucleotide sequences of the VGAM88 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM88 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM88 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM88 are further described hereinbelow with reference to Table 1.
- [1197] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM88 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1198] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 89 (VGAM89) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [1199] VGAM89 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM89 was detected is described

hereinabove with reference to Figs. 2–8.

[1200] VGAM89 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1201] VGAM89 gene, herein designated VGAM GENE, encodes a VGAM89 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM89 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM89 precursor RNA is designated SEQ ID:2053, and is provided hereinbelow with reference to the sequence listing part.

[1202] VGAM89 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM89 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1203] An enzyme complex designated DICER COMPLEX, dices the VGAM89 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM89 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM89 RNA is designated SEQ ID:2054, and is provided hereinbelow with reference to the sequence listing part.

[1204] VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.



[1205] VGAM89 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM89 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM89 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1206] The complementary binding of VGAM89 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM89 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1207] It is appreciated that VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM89 host target genes. The mRNA of each one of this plurality of VGAM89 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM89 RNA, herein designated VGAM RNA, and which when bound by VGAM89 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM89 host target proteins.

[1208] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM89 gene, herein designated VGAM GENE, on one or more VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known

non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1209] It is yet further appreciated that a function of VGAM89 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM89 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM89 correlate with, and may be deduced from, the identity of the host target genes which VGAM89 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1210] Nucleotide sequences of the VGAM89 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM89 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM89 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM89 are further described hereinbelow with reference to Table 1.

[1211] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM89 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1212] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 90 (VGAM90) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1213] VGAM90 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM90 was detected is described hereinabove with reference to Figs. 2-8.

[1214] VGAM90 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM90 host target gene, herein designated VGAM HOST

TARGET GENE, is a human gene contained in the human genome.

[1215] VGAM90 gene, herein designated VGAM GENE, encodes a VGAM90 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM90 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM90 precursor RNA is designated SEQ ID:2058, and is provided hereinbelow with reference to the sequence listing part.

[1216] VGAM90 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM90 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1217] An enzyme complex designated DICER COMPLEX, dices the VGAM90 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM90 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM90 RNA is designated SEQ ID:2059, and is provided hereinbelow with reference to the sequence listing part.

[1218] VGAM90 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1219] VGAM90 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM90 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM90 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1220] The complementary binding of VGAM90 RNA, herein designated VGAM RNA, to host target binding sites on VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM90 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1221] It is appreciated that VGAM90 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM90 host target genes. The mRNA of each one of this plurality of VGAM90 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM90 RNA, herein designated VGAM RNA, and which when bound by VGAM90 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM90 host target proteins.

[1222] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM90 gene, herein designated VGAM GENE, on one or more VGAM90 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and



Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1223] It is yet further appreciated that a function of VGAM90 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM90 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM90 correlate with, and may be deduced from, the identity of the host target genes which VGAM90 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1224] Nucleotide sequences of the VGAM90 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM90 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM90 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM90 are further described hereinbelow with reference to Table 1.

[1225] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM90 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1226] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 91 (VGAM91) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1227] VGAM91 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM91 was detected is described hereinabove with reference to Figs. 2-8.

[1228] VGAM91 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM91 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1229] VGAM91 gene, herein designated VGAM GENE, encodes a VGAM91 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM91 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM91 precursor RNA is designated SEQ ID:2091, and is provided hereinbelow with reference to the sequence listing part.

[1230] VGAM91 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM91 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1231] An enzyme complex designated DICER COMPLEX, dices the VGAM91 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM91 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM91 RNA is designated SEQ ID:2092, and is provided hereinbelow with reference to the sequence listing part.

[1232] VGAM91 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1233] VGAM91 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM91 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding

sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM91 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1234] The complementary binding of VGAM91 RNA, herein designated VGAM RNA, to host target binding sites on VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM91 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1235] It is appreciated that VGAM91 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM91 host target genes. The mRNA of each one of this plurality of VGAM91 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM91 RNA, herein designated VGAM RNA, and which when bound by VGAM91 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM91 host target proteins.

[1236] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM91 gene, herein designated VGAM GENE, on one or more VGAM91 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA

genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1237] It is yet further appreciated that a function of VGAM91 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM91 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM91 correlate with, and may be deduced from, the identity of the host target genes which VGAM91 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1238] Nucleotide sequences of the VGAM91 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM91 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM91 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM91 are further described hereinbelow with reference to Table 1.

[1239] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM91 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1240] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 92 (VGAM92) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1241] VGAM92 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM92 was detected is described hereinabove with reference to Figs. 2–8.

[1242] VGAM92 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1243] VGAM92 gene, herein designated VGAM GENE, encodes a VGAM92 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM92 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to



the nucleotide sequence of VGAM92 precursor RNA is designated SEQ ID:2095, and is provided hereinbelow with reference to the sequence listing part.

[1244] VGAM92 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM92 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1245] An enzyme complex designated DICER COMPLEX, dices the VGAM92 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM92 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM92 RNA is designated SEQ ID:2092, and is

provided hereinbelow with reference to the sequence listing part.

[1246] VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1247] VGAM92 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM92 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting VGAM92 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1248] The complementary binding of VGAM92 RNA, herein designated VGAM RNA, to host target binding sites on VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM92 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1249] It is appreciated that VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM92 host target genes. The mRNA of each one of this plurality of VGAM92 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM92 RNA, herein designated VGAM RNA, and which when bound by VGAM92 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM92 host target proteins.

[1250] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM92 gene, herein designated VGAM GENE, on one or more VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1251] It is yet further appreciated that a function of VGAM92 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM92 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM92 correlate with, and may be deduced from, the identity of the host target genes which VGAM92 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [1252] Nucleotide sequences of the VGAM92 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM92 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM92 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM92 are further described hereinbelow with reference to Table 1.
- [1253] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM92 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1254] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 93 (VGAM93) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1255] VGAM93 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM93 was detected is described hereinabove with reference to Figs. 2–8.

[1256] VGAM93 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1257] VGAM93 gene, herein designated VGAM GENE, encodes a VGAM93 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM93 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM93 precursor RNA is designated SEQ ID:2096, and is provided hereinbelow with reference to the sequence listing part.

[1258] VGAM93 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM93 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1259] An enzyme complex designated DICER COMPLEX, dices the VGAM93 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM93 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM93 RNA is designated SEQ ID:2097, and is provided hereinbelow with reference to the sequence listing part.

[1260] VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA,

VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1261] VGAM93 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM93 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM93 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM93 host target RNA, herein



designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1262] The complementary binding of VGAM93 RNA, herein designated VGAM RNA, to host target binding sites on VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM93 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1263] It is appreciated that VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM93 host target genes. The mRNA of each one of this plurality of VGAM93 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM93 RNA, herein designated VGAM RNA, and which when bound by VGAM93 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM93 host target proteins.

[1264] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM93 gene, herein designated VGAM GENE, on one or more VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1265] It is yet further appreciated that a function of VGAM93 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities,

of VGAM93 correlate with, and may be deduced from, the identity of the host target genes which VGAM93 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [1266] Nucleotide sequences of the VGAM93 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM93 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM93 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM93 are further described hereinbelow with reference to Table 1.
- [1267] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM93 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1268] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 94 (VGAM94) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1269] VGAM94 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM94 was detected is described hereinabove with reference to Figs. 2–8.

[1270] VGAM94 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1271] VGAM94 gene, herein designated VGAM GENE, encodes a VGAM94 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM94 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM94 precursor RNA is designated SEQ ID:2101, and is provided hereinbelow with reference to the sequence listing part.

[1272] VGAM94 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM94 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1273] An enzyme complex designated DICER COMPLEX, dices the VGAM94 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM94 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM94 RNA is designated SEQ ID:2102, and is provided hereinbelow with reference to the sequence listing part.

[1274] VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untrans-

lated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1275] VGAM94 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM94 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR re-

gion, the 5UTR region, or in both 3UTR and 5UTR regions.

[1276] The complementary binding of VGAM94 RNA, herein designated VGAM RNA, to host target binding sites on VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM94 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1277] It is appreciated that VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM94 host target genes. The mRNA of each one of this plurality of VGAM94 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM94 RNA, herein designated VGAM RNA, and which when bound by VGAM94 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM94 host target proteins.

[1278] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM94 gene, herein designated VGAM GENE, on one or more VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1279] It is yet further appreciated that a function of VGAM94 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM94 correlate with, and may be deduced from, the identity of the host target genes which VGAM94 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



- [1280] Nucleotide sequences of the VGAM94 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM94 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM94 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM94 are further described hereinbelow with reference to Table 1.
- [1281] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM94 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1282] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 95 (VGAM95) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [1283] VGAM95 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM95 was detected is described hereinabove with reference to Figs. 2-8.

[1284] VGAM95 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM95 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1285] VGAM95 gene, herein designated VGAM GENE, encodes a VGAM95 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM95 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM95 precursor RNA is designated SEQ ID:2116, and is provided hereinbelow with reference to the sequence listing part.

[1286] VGAM95 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM95 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[1287] An enzyme complex designated DICER COMPLEX, dices the VGAM95 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM95 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM95 RNA is designated SEQ ID:2117, and is provided hereinbelow with reference to the sequence listing part.

[1288] VGAM95 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1289] VGAM95 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM95 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1290] The complementary binding of VGAM95 RNA, herein designated VGAM RNA, to host target binding sites on VGAM95 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM95 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1291] It is appreciated that VGAM95 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM95 host target genes. The mRNA of each one of this plurality of VGAM95 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM95 RNA, herein designated VGAM RNA, and which when bound by VGAM95 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM95 host target proteins.

[1292] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM95 gene, herein designated VGAM GENE, on one or more VGAM95 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1293] It is yet further appreciated that a function of VGAM95 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM95 correlate with, and may be deduced from, the identity of the host target genes which VGAM95 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1294] Nucleotide sequences of the VGAM95 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM95 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM95 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM95 are further described hereinbelow with reference to Table 1.

[1295] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM95 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1296] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 96 (VGAM96) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1297] VGAM96 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM96 was detected is described hereinabove with reference to Figs. 2-8.

[1298] VGAM96 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human

genome.

[1299] VGAM96 gene, herein designated VGAM GENE, encodes a VGAM96 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM96 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM96 precursor RNA is designated SEQ ID:2147, and is provided hereinbelow with reference to the sequence listing part.

[1300] VGAM96 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM96 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1301] An enzyme complex designated DICER COMPLEX, dices the VGAM96 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM96 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM96 RNA is designated SEQ ID:2148, and is provided hereinbelow with reference to the sequence listing part.

[1302] VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1303] VGAM96 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide

sequence of VGAM96 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM96 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1304] The complementary binding of VGAM96 RNA, herein designated VGAM RNA, to host target binding sites on VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM96 host target protein, herein designated VGAM

HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1305] It is appreciated that VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM96 host target genes. The mRNA of each one of this plurality of VGAM96 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM96 RNA, herein designated VGAM RNA, and which when bound by VGAM96 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM96 host target proteins.

[1306] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM96 gene, herein designated VGAM GENE, on one or more VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1307] It is yet further appreciated that a function of VGAM96 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM96 correlate with, and may be deduced from, the identity of the host target genes which VGAM96 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1308] Nucleotide sequences of the VGAM96 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM96 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM96 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM96 are further described hereinbelow with reference to Table 1.

[1309] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM96 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1310] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 97 (VGAM97) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1311] VGAM97 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM97 was detected is described hereinabove with reference to Figs. 2-8.

[1312] VGAM97 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1313] VGAM97 gene, herein designated VGAM GENE, encodes a VGAM97 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM97 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM97 precursor RNA is designated SEQ ID:2160, and is provided hereinbelow with reference to the sequence listing part.

[1314] VGAM97 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM97 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1315] An enzyme complex designated DICER COMPLEX, dices the VGAM97 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM97 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM97 RNA is designated SEQ ID:2161, and is provided hereinbelow with reference to the sequence listing part.

[1316] VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1317] VGAM97 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM97 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target

binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM97 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1318] The complementary binding of VGAM97 RNA, herein designated VGAM RNA, to host target binding sites on VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM97 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1319] It is appreciated that VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM97 host target genes. The mRNA of each one of this plurality of VGAM97 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM97 RNA, herein designated VGAM RNA, and which when bound by VGAM97 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM97 host target proteins.

[1320] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM97 gene, herein designated VGAM GENE, on one or more VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective:

Glimpses of a tiny RNA world, Science 294,779 (2001)).

- [1321] It is yet further appreciated that a function of VGAM97 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM97 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM97 correlate with, and may be deduced from, the identity of the host target genes which VGAM97 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [1322] Nucleotide sequences of the VGAM97 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM97 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM97 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM97 are further described hereinbelow with reference to Table 1.
- [1323] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM97 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[1324] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 98 (VGAM98) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1325] VGAM98 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM98 was detected is described hereinabove with reference to Figs. 2–8.

[1326] VGAM98 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1327] VGAM98 gene, herein designated VGAM GENE, encodes a VGAM98 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM98 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM98 precursor RNA is

designated SEQ ID:2233, and is provided hereinbelow with reference to the sequence listing part.

[1328] VGAM98 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM98 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1329] An enzyme complex designated DICER COMPLEX, dices the VGAM98 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM98 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM98 RNA is designated SEQ ID:2234, and is provided hereinbelow with reference to the sequence list-

ing part.

[1330] VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1331] VGAM98 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing VGAM98 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1332] The complementary binding of VGAM98 RNA, herein designated VGAM RNA, to host target binding sites on VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM98 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1333] It is appreciated that VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM98 host target genes. The mRNA of each one of this plurality of VGAM98 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM98 RNA, herein designated VGAM RNA, and which when bound by VGAM98 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM98 host target proteins.

[1334] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM98 gene, herein designated VGAM GENE, on one or more VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1335] It is yet further appreciated that a function of VGAM98 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM98 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM98 correlate with, and may be deduced from, the identity of the host target genes which VGAM98 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [1336] Nucleotide sequences of the VGAM98 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM98 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM98 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM98 are further described hereinbelow with reference to Table 1.
- [1337] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM98 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1338] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 99 (VGAM99) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1339] VGAM99 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM99 was detected is described hereinabove with reference to Figs. 2–8.

[1340] VGAM99 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1341] VGAM99 gene, herein designated VGAM GENE, encodes a VGAM99 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM99 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM99 precursor RNA is designated SEQ ID:2246, and is provided hereinbelow with reference to the sequence listing part.

[1342] VGAM99 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM99 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1343] An enzyme complex designated DICER COMPLEX, dices the VGAM99 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM99 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM99 RNA is designated SEQ ID:2247, and is provided hereinbelow with reference to the sequence listing part.

[1344] VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM99 host target RNA, herein designated VGAM HOST

TARGET RNA. VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1345] VGAM99 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM99 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM99 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appre-

ciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1346] The complementary binding of VGAM99 RNA, herein designated VGAM RNA, to host target binding sites on VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM99 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1347] It is appreciated that VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM99 host target genes. The mRNA of each one of this plurality of VGAM99 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM99 RNA, herein designated VGAM RNA, and which when bound by VGAM99 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM99 host target proteins.

[1348] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM99 gene, herein designated VGAM GENE, on one or more VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1349] It is yet further appreciated that a function of VGAM99 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM99 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM99 correlate with, and may be deduced from, the identity of the

host target genes which VGAM99 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [1350] Nucleotide sequences of the VGAM99 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM99 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM99 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM99 are further described hereinbelow with reference to Table 1.
- [1351] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM99 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [1352] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 100 (VGAM100) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1353] VGAM100 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM100 was detected is described hereinabove with reference to Figs. 2–8.

[1354] VGAM100 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1355] VGAM100 gene, herein designated VGAM GENE, encodes a VGAM100 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM100 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM100 precursor RNA is designated SEQ ID:2250, and is provided hereinbelow with reference to the sequence listing part.

[1356] VGAM100 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1357] An enzyme complex designated DICER COMPLEX, dices the VGAM100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM100 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM100 RNA is designated SEQ ID:2251, and is provided hereinbelow with reference to the sequence listing part.

[1358] VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5



untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1359] VGAM100 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM100 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM100 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1360] The complementary binding of VGAM100 RNA, herein designated VGAM RNA, to host target binding sites on VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM100 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1361] It is appreciated that VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM100 host target genes. The mRNA of each one of this plurality of VGAM100 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM100 RNA, herein designated VGAM RNA, and which when bound by VGAM100 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM100 host target proteins.

[1362] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM100 gene, herein designated VGAM GENE, on one or more VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1363] It is yet further appreciated that a function of VGAM100 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM100 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM100 correlate with, and may be deduced from, the identity of the host target genes which VGAM100 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[1364] Nucleotide sequences of the VGAM100 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM100 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM100 are further described hereinbelow with reference to Table 1.

[1365] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM100 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1366] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 101 (VGAM101) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1367] VGAM101 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM101 was detected is described hereinabove with reference to Figs. 2–8.

[1368] VGAM101 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1369] VGAM101 gene, herein designated VGAM GENE, encodes a VGAM101 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM101 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM101 precursor RNA is designated SEQ ID:2271, and is provided hereinbelow with reference to the sequence listing part.

[1370] VGAM101 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1371] An enzyme complex designated DICER COMPLEX, dices the VGAM101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM101 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM101 RNA is designated SEQ ID:2272, and is provided hereinbelow with reference to the sequence listing part.

[1372] VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1373] VGAM101 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM101 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[1374] The complementary binding of VGAM101 RNA, herein designated VGAM RNA, to host target binding sites on VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM101 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1375] It is appreciated that VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM101 host target genes. The mRNA of each one of this plurality of VGAM101 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM101 RNA, herein designated VGAM RNA, and which when bound by VGAM101 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM101 host target proteins.

[1376] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM101 gene, herein designated VGAM GENE, on one or more VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1377] It is yet further appreciated that a function of VGAM101 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM101 correlate with, and may be deduced from, the identity of the host target genes which VGAM101 binds and inhibits, and the function of these host target

genes, as elaborated hereinbelow.

[1378] Nucleotide sequences of the VGAM101 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM101 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM101 are further described hereinbelow with reference to Table 1.

[1379] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM101 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1380] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 102 (VGAM102) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1381] VGAM102 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM102 was detected is described hereinabove with reference to Figs. 2–8.

[1382] VGAM102 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus.

VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1383] VGAM102 gene, herein designated VGAM GENE, encodes a VGAM102 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM102 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM102 precursor RNA is designated SEQ ID:2285, and is provided hereinbelow with reference to the sequence listing part.

[1384] VGAM102 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1385] An enzyme complex designated DICER COMPLEX, dices the VGAM102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM102 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM102 RNA is designated SEQ ID:2286, and is provided hereinbelow with reference to the sequence listing part.

[1386] VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[1387] VGAM102 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM102 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM102 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1388] The complementary binding of VGAM102 RNA, herein designated VGAM RNA, to host target binding sites on VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM102 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1389] It is appreciated that VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM102 host target genes. The mRNA of each one of this plurality of VGAM102 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM102 RNA, herein designated VGAM RNA, and which when bound by VGAM102 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM102 host target proteins.

[1390] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM102 gene, herein designated VGAM GENE, on one or

more VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1391] It is yet further appreciated that a function of VGAM102 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM102 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM102 correlate with, and may be deduced from, the identity of the host target genes which VGAM102 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1392] Nucleotide sequences of the VGAM102 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM102 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM102 are further described hereinbelow with reference to Table 1.

[1393] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM102 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1394] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 103 (VGAM103) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1395] VGAM103 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM103 was detected is described



hereinabove with reference to Figs. 2–8.

[1396] VGAM103 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM103 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1397] VGAM103 gene, herein designated VGAM GENE, encodes a VGAM103 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM103 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM103 precursor RNA is designated SEQ ID:2290, and is provided hereinbelow with reference to the sequence listing part.

[1398] VGAM103 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1399] An enzyme complex designated DICER COMPLEX, dices the VGAM103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM103 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM103 RNA is designated SEQ ID:2291, and is provided hereinbelow with reference to the sequence listing part.

[1400] VGAM103 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1401] VGAM103 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM103 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1402] The complementary binding of VGAM103 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM103 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1403] It is appreciated that VGAM103 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM103 host target genes. The mRNA of each one of this plurality of VGAM103 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM103 RNA, herein designated VGAM RNA, and which when bound by VGAM103 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM103 host target proteins.

[1404] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM103 gene, herein designated VGAM GENE, on one or more VGAM103 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1405] It is yet further appreciated that a function of VGAM103 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM103 correlate with, and may be deduced from, the identity of the host target genes which VGAM103 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1406] Nucleotide sequences of the VGAM103 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM103 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM103 are further described hereinbelow with reference to Table 1.

[1407] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM103 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1408] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 104 (VGAM104) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1409] VGAM104 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM104 was detected is described hereinabove with reference to Figs. 2-8.

[1410] VGAM104 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM104 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1411] VGAM104 gene, herein designated VGAM GENE, encodes a VGAM104 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM104 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM104 precursor RNA is designated SEQ ID:2311, and is provided hereinbelow with reference to the sequence listing part.

[1412] VGAM104 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

- [1413] An enzyme complex designated DICER COMPLEX, dices the VGAM104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM104 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM104 RNA is designated SEQ ID:2312, and is provided hereinbelow with reference to the sequence listing part.
- [1414] VGAM104 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.
- [1415] VGAM104 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM104 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM104 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1416] The complementary binding of VGAM104 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM104 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1417] It is appreciated that VGAM104 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM104 host target genes. The mRNA of each one of this plurality of VGAM104 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM104 RNA, herein designated VGAM RNA, and which when bound by VGAM104 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM104 host target proteins.

[1418] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM104 gene, herein designated VGAM GENE, on one or more VGAM104 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1419] It is yet further appreciated that a function of VGAM104 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM104 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM104 correlate with, and may be deduced from, the identity of the host target genes which VGAM104 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1420] Nucleotide sequences of the VGAM104 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM104 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM104 are further described hereinbelow with reference to Table 1.

[1421] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM104 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1422] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 105 (VGAM105) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1423] VGAM105 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM105 was detected is described hereinabove with reference to Figs. 2-8.

[1424] VGAM105 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine herpesvirus 2. VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1425] VGAM105 gene, herein designated VGAM GENE, encodes a VGAM105 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM105 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM105 precursor RNA is designated SEQ ID:2331, and is provided hereinbelow with reference to the sequence listing part.

[1426] VGAM105 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

- [1427] An enzyme complex designated DICER COMPLEX, dices the VGAM105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM105 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM105 RNA is designated SEQ ID:2332, and is provided hereinbelow with reference to the sequence listing part.
- [1428] VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.
- [1429] VGAM105 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM105 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM105 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1430] The complementary binding of VGAM105 RNA, herein designated VGAM RNA, to host target binding sites on VGAM105 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM105 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1431] It is appreciated that VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM105 host target genes. The mRNA of each one of this plurality of VGAM105 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM105 RNA, herein designated VGAM RNA, and which when bound by VGAM105 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM105 host target proteins.

[1432] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM105 gene, herein designated VGAM GENE, on one or more VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1433] It is yet further appreciated that a function of VGAM105 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM105 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM105 correlate with, and may be deduced from, the identity of the host target genes which VGAM105 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1434] Nucleotide sequences of the VGAM105 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM105 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM105 are further described hereinbelow with reference to Table 1.

[1435] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM105 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1436] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 106 (VGAM106) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1437] VGAM106 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM106 was detected is described hereinabove with reference to Figs. 2-8.

[1438] VGAM106 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2.

VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1439] VGAM106 gene, herein designated VGAM GENE, encodes a VGAM106 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM106 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM106 precursor RNA is designated SEQ ID:2342, and is provided hereinbelow with reference to the sequence listing part.

[1440] VGAM106 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1441] An enzyme complex designated DICER COMPLEX, dices

the VGAM106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM106 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM106 RNA is designated SEQ ID:2343, and is provided hereinbelow with reference to the sequence listing part.

[1442] VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1443] VGAM106 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM106 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM106 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1444] The complementary binding of VGAM106 RNA, herein designated VGAM RNA, to host target binding sites on VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM106 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1445] It is appreciated that VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM106 host target genes. The mRNA of each one of this plurality of VGAM106 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM106 RNA, herein designated VGAM RNA, and which when bound by VGAM106 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM106 host target proteins.

[1446] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM106 gene, herein designated VGAM GENE, on one or more VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1447] It is yet further appreciated that a function of VGAM106 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM106 correlate with, and may be deduced from, the identity of the host target genes which VGAM106 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1448] Nucleotide sequences of the VGAM106 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM106 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM106 are further described hereinbelow with reference to Table 1.

[1449] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM106 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1450] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 107 (VGAM107) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1451] VGAM107 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM107 was detected is described hereinabove with reference to Figs. 2-8.

[1452] VGAM107 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM107 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[1453] VGAM107 gene, herein designated VGAM GENE, encodes a VGAM107 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM107 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM107 precursor RNA is designated SEQ ID:2347, and is provided hereinbelow with reference to the sequence listing part.

[1454] VGAM107 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1455] An enzyme complex designated DICER COMPLEX, dices the VGAM107 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM107 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM107 RNA is designated SEQ ID:2348, and is provided hereinbelow with reference to the sequence listing part.

[1456] VGAM107 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1457] VGAM107 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM107 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1458] The complementary binding of VGAM107 RNA, herein designated VGAM RNA, to host target binding sites on VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM107 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM107 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1459] It is appreciated that VGAM107 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM107 host target genes. The mRNA of each one of this plurality of VGAM107 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM107 RNA, herein designated VGAM RNA, and which when bound by VGAM107 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM107 host target proteins.

[1460] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM107 gene, herein designated VGAM GENE, on one or more VGAM107 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1461] It is yet further appreciated that a function of VGAM107 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM107 correlate with, and may be deduced from, the identity of the host target genes which VGAM107 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1462] Nucleotide sequences of the VGAM107 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM107 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM107 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM107 are further described hereinbelow with reference to Table 1.

[1463] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM107 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1464] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 108 (VGAM108) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1465] VGAM108 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM108 was detected is described hereinabove with reference to Figs. 2-8.

[1466] VGAM108 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[1467] VGAM108 gene, herein designated VGAM GENE, encodes a VGAM108 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM108 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM108 precursor RNA is designated SEQ ID:2377, and is provided hereinbelow with reference to the sequence listing part.

[1468] VGAM108 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1469] An enzyme complex designated DICER COMPLEX, dices the VGAM108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM108 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM108 RNA is designated SEQ ID:2378, and is provided hereinbelow with reference to the sequence listing part.

[1470] VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1471] VGAM108 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM108 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM108 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1472] The complementary binding of VGAM108 RNA, herein designated VGAM RNA, to host target binding sites on VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM108 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1473] It is appreciated that VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM108 host target genes. The mRNA of each one of this plurality of VGAM108 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM108 RNA, herein designated VGAM RNA, and which when bound by VGAM108 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM108 host target proteins.

[1474] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM108 gene, herein designated VGAM GENE, on one or more VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1475] It is yet further appreciated that a function of VGAM108 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM108 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM108 correlate with, and may be deduced from, the identity of the host target genes which VGAM108 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1476] Nucleotide sequences of the VGAM108 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM108 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM108 are further de-

scribed hereinbelow with reference to Table 1.

[1477] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM108 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1478] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 109 (VGAM109) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1479] VGAM109 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM109 was detected is described hereinabove with reference to Figs. 2-8.

[1480] VGAM109 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1481] VGAM109 gene, herein designated VGAM GENE, encodes a VGAM109 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM109 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM109 precursor RNA is designated SEQ ID:2385, and is provided hereinbelow with reference to the sequence listing part.

[1482] VGAM109 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1483] An enzyme complex designated DICER COMPLEX, dices the VGAM109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM109 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM109 RNA is designated SEQ ID:2386, and is provided hereinbelow with reference to the sequence listing part.

[1484] VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1485] VGAM109 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM109 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM109 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1486] The complementary binding of VGAM109 RNA, herein designated VGAM RNA, to host target binding sites on VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM109 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1487] It is appreciated that VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM109 host target genes. The mRNA of each one of this plurality of VGAM109 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM109 RNA, herein designated VGAM RNA, and which when bound by VGAM109 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM109 host target proteins.

[1488] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM109 gene, herein designated VGAM GENE, on one or more VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1489] It is yet further appreciated that a function of VGAM109 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM109 correlate with, and may be deduced from, the identity of the host target genes which VGAM109 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1490] Nucleotide sequences of the VGAM109 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM109 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM109 are further described hereinbelow with reference to Table 1.

[1491] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM109 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1492] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 110 (VGAM110) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1493] VGAM110 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM110 was detected is described hereinabove with reference to Figs. 2-8.

[1494] VGAM110 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1495] VGAM110 gene, herein designated VGAM GENE, encodes a

VGAM110 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM110 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM110 precursor RNA is designated SEQ ID:2391, and is provided hereinbelow with reference to the sequence listing part.

[1496] VGAM110 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1497] An enzyme complex designated DICER COMPLEX, dices the VGAM110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM110 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM110 RNA is designated SEQ ID:2392, and is provided hereinbelow with reference to the sequence listing part.

[1498] VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1499] VGAM110 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM110 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1500] The complementary binding of VGAM110 RNA, herein designated VGAM RNA, to host target binding sites on VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM110 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[1501] It is appreciated that VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM110 host target genes. The mRNA of each one of this plurality of VGAM110 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM110 RNA, herein designated VGAM RNA, and which when bound by VGAM110 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM110 host target proteins.

[1502] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM110 gene, herein designated VGAM GENE, on one or more VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1503] It is yet further appreciated that a function of VGAM110 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM110 correlate with, and may be deduced from, the identity of the host target genes which VGAM110 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1504] Nucleotide sequences of the VGAM110 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM110 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM110 are further described hereinbelow with reference to Table 1.

[1505] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM110 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1506] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 111 (VGAM111) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1507] VGAM111 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM111 was detected is described hereinabove with reference to Figs. 2-8.

[1508] VGAM111 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM111 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1509] VGAM111 gene, herein designated VGAM GENE, encodes a VGAM111 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM111 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM111 precursor RNA is designated SEQ ID:2412, and is provided hereinbelow with reference to the sequence listing part.

[1510] VGAM111 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1511] An enzyme complex designated DICER COMPLEX, dices the VGAM111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM111 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM111 RNA is designated SEQ ID:2413, and is provided hereinbelow with reference to the sequence listing part.

[1512] VGAM111 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1513] VGAM111 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM111 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1514] The complementary binding of VGAM111 RNA, herein designated VGAM RNA, to host target binding sites on VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM111 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1515] It is appreciated that VGAM111 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM111 host target genes. The mRNA of each one of this plurality of VGAM111 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM111 RNA, herein designated VGAM RNA, and which when bound by VGAM111 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM111 host target proteins.

[1516] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM111 gene, herein designated VGAM GENE, on one or more VGAM111 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1517] It is yet further appreciated that a function of VGAM111 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM111 correlate with, and may be deduced from, the identity of the host target genes which VGAM111 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1518] Nucleotide sequences of the VGAM111 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM111 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM111 are further described hereinbelow with reference to Table 1.

[1519] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM111 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1520] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 112 (VGAM112) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1521] VGAM112 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM112 was detected is described hereinabove with reference to Figs. 2–8.

[1522] VGAM112 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM112 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1523] VGAM112 gene, herein designated VGAM GENE, encodes a VGAM112 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM112 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM112 precursor RNA is designated SEQ ID:2427, and is provided hereinbelow with reference to the sequence listing part.

[1524] VGAM112 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1525] An enzyme complex designated DICER COMPLEX, dices the VGAM112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM112 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM112 RNA is designated SEQ ID:2428, and is provided hereinbelow with reference to the sequence listing part.

[1526] VGAM112 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1527] VGAM112 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM112 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1528] The complementary binding of VGAM112 RNA, herein designated VGAM RNA, to host target binding sites on VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM112 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1529] It is appreciated that VGAM112 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM112 host target genes. The mRNA of each one of this plurality of VGAM112 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM112 RNA, herein designated VGAM RNA, and which when bound by VGAM112 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM112 host target proteins.

[1530] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM112 gene, herein designated VGAM GENE, on one or more VGAM112 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1531] It is yet further appreciated that a function of VGAM112 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM112 correlate with, and may be deduced from, the identity of the host target genes which VGAM112 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1532] Nucleotide sequences of the VGAM112 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM112 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM112 are further described hereinbelow with reference to Table 1.

[1533] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM112 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1534] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 113 (VGAM113) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1535] VGAM113 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM113 was detected is described hereinabove with reference to Figs. 2–8.

[1536] VGAM113 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM113 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1537] VGAM113 gene, herein designated VGAM GENE, encodes a VGAM113 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM113 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM113 precursor RNA is designated SEQ ID:2432, and is provided hereinbelow with reference to the sequence listing part.

[1538] VGAM113 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1539] An enzyme complex designated DICER COMPLEX, dices the VGAM113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM113 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM113 RNA is designated SEQ ID:2433, and is provided hereinbelow with reference to the sequence listing part.

[1540] VGAM113 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1541] VGAM113 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM113 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1542] The complementary binding of VGAM113 RNA, herein designated VGAM RNA, to host target binding sites on VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM113 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1543] It is appreciated that VGAM113 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM113 host target genes. The mRNA of each one of this plurality of VGAM113 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM113 RNA, herein designated VGAM RNA, and which when bound by VGAM113 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM113 host target proteins.

[1544] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM113 gene, herein designated VGAM GENE, on one or more VGAM113 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [1545] It is yet further appreciated that a function of VGAM113 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM113 correlate with, and may be deduced from, the identity of the host target genes which VGAM113 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [1546] Nucleotide sequences of the VGAM113 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM113 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM113 are further described hereinbelow with reference to Table 1.
- [1547] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM113 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1548] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 114 (VGAM114) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1549] VGAM114 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM114 was detected is described hereinabove with reference to Figs. 2–8.

[1550] VGAM114 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1551] VGAM114 gene, herein designated VGAM GENE, encodes a VGAM114 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM114 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM114 precursor RNA is designated SEQ ID:2445, and is provided hereinbelow with reference to the sequence listing part.

[1552] VGAM114 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1553] An enzyme complex designated DICER COMPLEX, dices the VGAM114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM114 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM114 RNA is designated SEQ ID:2446, and is provided hereinbelow with reference to the sequence listing part.

[1554] VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1555] VGAM114 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM114 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1556] The complementary binding of VGAM114 RNA, herein designated VGAM RNA, to host target binding sites on VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM114 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1557] It is appreciated that VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM114 host target genes. The mRNA of

each one of this plurality of VGAM114 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM114 RNA, herein designated VGAM RNA, and which when bound by VGAM114 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM114 host target proteins.

[1558] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM114 gene, herein designated VGAM GENE, on one or more VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[1559] It is yet further appreciated that a function of VGAM114 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM114 correlate with, and may be deduced from, the identity of the host target genes which VGAM114 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1560] Nucleotide sequences of the VGAM114 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM114 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM114 are further described hereinbelow with reference to Table 1.

[1561] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM114 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[1562] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 115 (VGAM115) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1563] VGAM115 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM115 was detected is described hereinabove with reference to Figs. 2–8.

[1564] VGAM115 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1565] VGAM115 gene, herein designated VGAM GENE, encodes a VGAM115 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM115 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar



to the nucleotide sequence of VGAM115 precursor RNA is designated SEQ ID:2459, and is provided hereinbelow with reference to the sequence listing part.

[1566] VGAM115 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1567] An enzyme complex designated DICER COMPLEX, dices the VGAM115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM115 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM115 RNA is designated SEQ ID:2460, and

is provided hereinbelow with reference to the sequence listing part.

[1568] VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1569] VGAM115 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM115 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1570] The complementary binding of VGAM115 RNA, herein designated VGAM RNA, to host target binding sites on VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM115 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1571] It is appreciated that VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM115 host target genes. The mRNA of each one of this plurality of VGAM115 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM115 RNA, herein designated VGAM RNA, and which when bound by VGAM115 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM115 host target proteins.

[1572] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM115 gene, herein designated VGAM GENE, on one or more VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1573] It is yet further appreciated that a function of VGAM115 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM115 correlate with, and may be deduced from, the identity of the host target genes which VGAM115 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1574] Nucleotide sequences of the VGAM115 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM115 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM115 are further described hereinbelow with reference to Table 1.

[1575] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM115 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1576] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 116 (VGAM116) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1577] VGAM116 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM116 was detected is described hereinabove with reference to Figs. 2–8.

[1578] VGAM116 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1579] VGAM116 gene, herein designated VGAM GENE, encodes a VGAM116 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM116 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM116 precursor RNA is

designated SEQ ID:2521, and is provided hereinbelow with reference to the sequence listing part.

[1580] VGAM116 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1581] An enzyme complex designated DICER COMPLEX, dices the VGAM116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM116 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM116 RNA is designated SEQ ID:2522, and is provided hereinbelow with reference to the sequence

listing part.

[1582] VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1583] VGAM116 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM116 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM116 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1584] The complementary binding of VGAM116 RNA, herein designated VGAM RNA, to host target binding sites on VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM116 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1585] It is appreciated that VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM116 host target genes. The mRNA of each one of this plurality of VGAM116 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM116 RNA, herein designated VGAM RNA, and which when bound by VGAM116 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM116 host target proteins.

[1586] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM116 gene, herein designated VGAM GENE, on one or more VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1587] It is yet further appreciated that a function of VGAM116 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM116 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM116 correlate with, and may be deduced from, the identity of the host target genes which VGAM116 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1588] Nucleotide sequences of the VGAM116 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM116 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM116 are further described hereinbelow with reference to Table 1.

[1589] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM116 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1590] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 117 (VGAM117) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1591] VGAM117 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM117 was detected is described hereinabove with reference to Figs. 2–8.

[1592] VGAM117 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1593] VGAM117 gene, herein designated VGAM GENE, encodes a VGAM117 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM117 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM117 precursor RNA is designated SEQ ID:2529, and is provided hereinbelow with

reference to the sequence listing part.

[1594] VGAM117 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1595] An enzyme complex designated DICER COMPLEX, dices the VGAM117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM117 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM117 RNA is designated SEQ ID:2530, and is provided hereinbelow with reference to the sequence listing part.

[1596] VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1597] VGAM117 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM117 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM117 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1598] The complementary binding of VGAM117 RNA, herein designated VGAM RNA, to host target binding sites on VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM117 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1599] It is appreciated that VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM117 host target genes. The mRNA of each one of this plurality of VGAM117 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM117 RNA, herein designated VGAM RNA, and which when bound by VGAM117 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM117 host target proteins.

[1600] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM117 gene, herein designated VGAM GENE, on one or more VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1601] It is yet further appreciated that a function of VGAM117 is inhibition of expression of host target genes, as part of a



novel viral mechanism of attacking a host. Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM117 correlate with, and may be deduced from, the identity of the host target genes which VGAM117 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1602] Nucleotide sequences of the VGAM117 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM117 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM117 are further described hereinbelow with reference to Table 1.

[1603] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM117 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1604] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 118 (VGAM118) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1605] VGAM118 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM118 was detected is described hereinabove with reference to Figs. 2–8.

[1606] VGAM118 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM118 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1607] VGAM118 gene, herein designated VGAM GENE, encodes a VGAM118 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM118 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM118 precursor RNA is designated SEQ ID:2547, and is provided hereinbelow with reference to the sequence listing part.

[1608] VGAM118 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1609] An enzyme complex designated DICER COMPLEX, dices the VGAM118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM118 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM118 RNA is designated SEQ ID:2548, and is provided hereinbelow with reference to the sequence listing part.

[1610] VGAM118 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1611] VGAM118 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM118 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM118 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1612] The complementary binding of VGAM118 RNA, herein designated VGAM RNA, to host target binding sites on VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM118 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1613] It is appreciated that VGAM118 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM118 host target genes. The mRNA of each one of this plurality of VGAM118 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM118 RNA, herein designated VGAM

RNA, and which when bound by VGAM118 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM118 host target proteins.

[1614] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM118 gene, herein designated VGAM GENE, on one or more VGAM118 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1615] It is yet further appreciated that a function of VGAM118 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM118 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM118 correlate with, and may be deduced from, the identity of the host target genes which VGAM118 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1616] Nucleotide sequences of the VGAM118 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM118 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM118 are further described hereinbelow with reference to Table 1.

[1617] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM118 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1618] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 119 (VGAM119) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1619] VGAM119 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM119 was detected is described hereinabove with reference to Figs. 2–8.

[1620] VGAM119 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1621] VGAM119 gene, herein designated VGAM GENE, encodes a VGAM119 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM119 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM119 precursor RNA is designated SEQ ID:2610, and is provided hereinbelow with reference to the sequence listing part.

[1622] VGAM119 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1623] An enzyme complex designated DICER COMPLEX, dices the VGAM119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM119 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM119 RNA is designated SEQ ID:2611, and is provided hereinbelow with reference to the sequence listing part.

[1624] VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1625] VGAM119 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM119 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM119 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1626] The complementary binding of VGAM119 RNA, herein designated VGAM RNA, to host target binding sites on VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM119 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1627] It is appreciated that VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM119 host target genes. The mRNA of each one of this plurality of VGAM119 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM119 RNA, herein designated VGAM RNA, and which when bound by VGAM119 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM119 host target proteins.

[1628] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM119 gene, herein designated VGAM GENE, on one or more VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1629] It is yet further appreciated that a function of VGAM119 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM119 include diagnosis, prevention and

treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM119 correlate with, and may be deduced from, the identity of the host target genes which VGAM119 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1630] Nucleotide sequences of the VGAM119 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM119 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM119 are further described hereinbelow with reference to Table 1.

[1631] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM119 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1632] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 120 (VGAM120) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1633] VGAM120 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM120 was detected is described hereinabove with reference to Figs. 2–8.

[1634] VGAM120 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1635] VGAM120 gene, herein designated VGAM GENE, encodes a VGAM120 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM120 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM120 precursor RNA is designated SEQ ID:2632, and is provided hereinbelow with reference to the sequence listing part.

[1636] VGAM120 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM120 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1637] An enzyme complex designated DICER COMPLEX, dices the VGAM120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM120 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM120 RNA is designated SEQ ID:2633, and is provided hereinbelow with reference to the sequence listing part.

[1638] VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM120 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1639] VGAM120 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM120 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1640] The complementary binding of VGAM120 RNA, herein designated VGAM RNA, to host target binding sites on VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM120 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1641] It is appreciated that VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM120 host target genes. The mRNA of each one of this plurality of VGAM120 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM120 RNA, herein designated VGAM RNA, and which when bound by VGAM120 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM120 host target proteins.

[1642] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM120 gene, herein designated VGAM GENE, on one or more VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1643] It is yet further appreciated that a function of VGAM120 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadi-

novirus. Specific functions, and accordingly utilities, of VGAM120 correlate with, and may be deduced from, the identity of the host target genes which VGAM120 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1644] Nucleotide sequences of the VGAM120 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM120 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM120 are further described hereinbelow with reference to Table 1.

[1645] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM120 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1646] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 121 (VGAM121) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[1647] VGAM121 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM121 was detected is described hereinabove with reference to Figs. 2–8.

[1648] VGAM121 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM121 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1649] VGAM121 gene, herein designated VGAM GENE, encodes a VGAM121 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM121 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM121 precursor RNA is designated SEQ ID:2676, and is provided hereinbelow with reference to the sequence listing part.

[1650] VGAM121 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM121 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1651] An enzyme complex designated DICER COMPLEX, dices the VGAM121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM121 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM121 RNA is designated SEQ ID:2677, and is provided hereinbelow with reference to the sequence listing part.

[1652] VGAM121 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM121 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1653] VGAM121 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM121 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1654] The complementary binding of VGAM121 RNA, herein designated VGAM RNA, to host target binding sites on VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM121 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1655] It is appreciated that VGAM121 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM121 host target genes. The mRNA of each one of this plurality of VGAM121 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM121 RNA, herein designated VGAM RNA, and which when bound by VGAM121 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM121 host target proteins.

[1656] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM121 gene, herein designated VGAM GENE, on one or more VGAM121 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1657] It is yet further appreciated that a function of VGAM121 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM121



correlate with, and may be deduced from, the identity of the host target genes which VGAM121 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1658] Nucleotide sequences of the VGAM121 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM121 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM121 are further described hereinbelow with reference to Table 1.

[1659] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM121 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1660] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 122 (VGAM122) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[1661] VGAM122 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM122 was detected is described hereinabove with reference to Figs. 2–8.

[1662] VGAM122 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM122 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1663] VGAM122 gene, herein designated VGAM GENE, encodes a VGAM122 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM122 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM122 precursor RNA is designated SEQ ID:2698, and is provided hereinbelow with reference to the sequence listing part.

[1664] VGAM122 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1665] An enzyme complex designated DICER COMPLEX, dices the VGAM122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM122 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM122 RNA is designated SEQ ID:2699, and is provided hereinbelow with reference to the sequence listing part.

[1666] VGAM122 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1667] VGAM122 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM122 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1668] The complementary binding of VGAM122 RNA, herein designated VGAM RNA, to host target binding sites on VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM122 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1669] It is appreciated that VGAM122 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM122 host target genes. The mRNA of each one of this plurality of VGAM122 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM122 RNA, herein designated VGAM RNA, and which when bound by VGAM122 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM122 host target proteins.

[1670] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM122 gene, herein designated VGAM GENE, on one or more VGAM122 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1671] It is yet further appreciated that a function of VGAM122 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of viral infection by Macaca mulatta rhadinovirus. Specific functions, and accordingly utilities, of VGAM122 correlate with, and may be deduced from, the

identity of the host target genes which VGAM122 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1672] Nucleotide sequences of the VGAM122 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM122 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM122 are further described hereinbelow with reference to Table 1.

[1673] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM122 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1674] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 123 (VGAM123) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1675] VGAM123 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM123 was detected is described hereinabove with reference to Figs. 2–8.

[1676] VGAM123 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM123 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1677] VGAM123 gene, herein designated VGAM GENE, encodes a VGAM123 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM123 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM123 precursor RNA is designated SEQ ID:2713, and is provided hereinbelow with reference to the sequence listing part.

[1678] VGAM123 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1679] An enzyme complex designated DICER COMPLEX, dices the VGAM123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM123 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM123 RNA is designated SEQ ID:2714, and is provided hereinbelow with reference to the sequence listing part.

[1680] VGAM123 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1681] VGAM123 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM123 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM123 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1682] The complementary binding of VGAM123 RNA, herein designated VGAM RNA, to host target binding sites on VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM123 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1683] It is appreciated that VGAM123 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM123 host target genes. The mRNA of each one of this plurality of VGAM123 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM123 RNA, herein designated VGAM RNA, and which when bound by VGAM123 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM123 host target proteins.

[1684] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM123 gene, herein designated VGAM GENE, on one or more VGAM123 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1685] It is yet further appreciated that a function of VGAM123 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM123 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM123 correlate with, and may be deduced from, the identity of the host target genes which VGAM123 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[1686] Nucleotide sequences of the VGAM123 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM123 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM123 are further described hereinbelow with reference to Table 1.

[1687] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM123 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1688] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 124 (VGAM124) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1689] VGAM124 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM124 was detected is described hereinabove with reference to Figs. 2–8.

[1690] VGAM124 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1691] VGAM124 gene, herein designated VGAM GENE, encodes a VGAM124 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM124 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM124 precursor RNA is designated SEQ ID:2718, and is provided hereinbelow with reference to the sequence listing part.

[1692] VGAM124 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1693] An enzyme complex designated DICER COMPLEX, dices the VGAM124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM124 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM124 RNA is designated SEQ ID:2719, and is provided hereinbelow with reference to the sequence listing part.

[1694] VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1695] VGAM124 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM124 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[1696] The complementary binding of VGAM124 RNA, herein designated VGAM RNA, to host target binding sites on VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM124 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1697] It is appreciated that VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM124 host target genes. The mRNA of each one of this plurality of VGAM124 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM124 RNA, herein designated VGAM RNA, and which when bound by VGAM124 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM124 host target proteins.

[1698] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM124 gene, herein designated VGAM GENE, on one or more VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1699] It is yet further appreciated that a function of VGAM124 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM124 correlate with, and may be deduced from, the identity of the host target genes which VGAM124 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[1700] Nucleotide sequences of the VGAM124 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM124 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM124 are further described hereinbelow with reference to Table 1.

[1701] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM124 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1702] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 125 (VGAM125) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1703] VGAM125 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM125 was detected is described hereinabove with reference to Figs. 2–8.

[1704] VGAM125 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1705] VGAM125 gene, herein designated VGAM GENE, encodes a VGAM125 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM125 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM125 precursor RNA is designated SEQ ID:2737, and is provided hereinbelow with reference to the sequence listing part.

[1706] VGAM125 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1707] An enzyme complex designated DICER COMPLEX, dices the VGAM125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM125 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM125 RNA is designated SEQ ID:2738, and is provided hereinbelow with reference to the sequence listing part.

[1708] VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[1709] VGAM125 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM125 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1710] The complementary binding of VGAM125 RNA, herein designated VGAM RNA, to host target binding sites on VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM125 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1711] It is appreciated that VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM125 host target genes. The mRNA of each one of this plurality of VGAM125 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM125 RNA, herein designated VGAM RNA, and which when bound by VGAM125 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM125 host target proteins.

[1712] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM125 gene, herein designated VGAM GENE, on one or

more VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1713] It is yet further appreciated that a function of VGAM125 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM125 correlate with, and may be deduced from, the identity of the host target genes which VGAM125 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[1714] Nucleotide sequences of the VGAM125 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM125 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM125 are further described hereinbelow with reference to Table 1.

[1715] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM125 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1716] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 126 (VGAM126) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1717] VGAM126 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM126 was detected is described

hereinabove with reference to Figs. 2–8.

[1718] VGAM126 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM126 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1719] VGAM126 gene, herein designated VGAM GENE, encodes a VGAM126 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM126 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM126 precursor RNA is designated SEQ ID:2775, and is provided hereinbelow with reference to the sequence listing part.

[1720] VGAM126 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1721] An enzyme complex designated DICER COMPLEX, dices the VGAM126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM126 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM126 RNA is designated SEQ ID:2776, and is provided hereinbelow with reference to the sequence listing part.

[1722] VGAM126 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1723] VGAM126 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM126 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1724] The complementary binding of VGAM126 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM126 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1725] It is appreciated that VGAM126 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM126 host target genes. The mRNA of each one of this plurality of VGAM126 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM126 RNA, herein designated VGAM RNA, and which when bound by VGAM126 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM126 host target proteins.

[1726] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM126 gene, herein designated VGAM GENE, on one or more VGAM126 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1727] It is yet further appreciated that a function of VGAM126 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM126 correlate with, and may be deduced from, the identity of the host target genes which VGAM126 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1728] Nucleotide sequences of the VGAM126 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM126 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM126 are further described hereinbelow with reference to Table 1.

[1729] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM126 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1730] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 127 (VGAM127) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1731] VGAM127 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM127 was detected is described hereinabove with reference to Figs. 2-8.

[1732] VGAM127 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1733] VGAM127 gene, herein designated VGAM GENE, encodes a VGAM127 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM127 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM127 precursor RNA is designated SEQ ID:2781, and is provided hereinbelow with reference to the sequence listing part.

[1734] VGAM127 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

- [1735] An enzyme complex designated DICER COMPLEX, dices the VGAM127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM127 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM127 RNA is designated SEQ ID:2782, and is provided hereinbelow with reference to the sequence listing part.
- [1736] VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.
- [1737] VGAM127 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM127 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1738] The complementary binding of VGAM127 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM127 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1739] It is appreciated that VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM127 host target genes. The mRNA of each one of this plurality of VGAM127 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM127 RNA, herein designated VGAM RNA, and which when bound by VGAM127 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM127 host target proteins.

[1740] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM127 gene, herein designated VGAM GENE, on one or more VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1741] It is yet further appreciated that a function of VGAM127 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM127 correlate with, and may be deduced from, the identity of the host target genes which VGAM127 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1742] Nucleotide sequences of the VGAM127 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM127 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM127 are further described hereinbelow with reference to Table 1.

[1743] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM127 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1744] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 128 (VGAM128) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1745] VGAM128 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM128 was detected is described hereinabove with reference to Figs. 2-8.

[1746] VGAM128 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Cryphonectria hypovirus. VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1747] VGAM128 gene, herein designated VGAM GENE, encodes a VGAM128 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM128 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM128 precursor RNA is designated SEQ ID:2796, and is provided hereinbelow with reference to the sequence listing part.

[1748] VGAM128 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1749] An enzyme complex designated DICER COMPLEX, dices the VGAM128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM128 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM128 RNA is designated SEQ ID:2797, and is provided hereinbelow with reference to the sequence listing part.

[1750] VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1751] VGAM128 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM128 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1752] The complementary binding of VGAM128 RNA, herein designated VGAM RNA, to host target binding sites on VGAM128 host target RNA, herein designated VGAM HOST



TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM128 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1753] It is appreciated that VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM128 host target genes. The mRNA of each one of this plurality of VGAM128 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM128 RNA, herein designated VGAM RNA, and which when bound by VGAM128 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM128 host target proteins.

[1754] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM128 gene, herein designated VGAM GENE, on one or more VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1755] It is yet further appreciated that a function of VGAM128 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM128 correlate with, and may be deduced from, the identity of the host target genes which VGAM128 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1756] Nucleotide sequences of the VGAM128 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM128 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM128 are further described hereinbelow with reference to Table 1.

[1757] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM128 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1758] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 129 (VGAM129) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1759] VGAM129 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM129 was detected is described hereinabove with reference to Figs. 2-8.

[1760] VGAM129 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus

1. VGAM129 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1761] VGAM129 gene, herein designated VGAM GENE, encodes a VGAM129 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM129 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM129 precursor RNA is designated SEQ ID:2828, and is provided hereinbelow with reference to the sequence listing part.

[1762] VGAM129 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1763] An enzyme complex designated DICER COMPLEX, dices

the VGAM129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM129 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM129 RNA is designated SEQ ID:2829, and is provided hereinbelow with reference to the sequence listing part.

[1764] VGAM129 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1765] VGAM129 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM129 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM129 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM129 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1766] The complementary binding of VGAM129 RNA, herein designated VGAM RNA, to host target binding sites on VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM129 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1767] It is appreciated that VGAM129 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM129 host target genes. The mRNA of each one of this plurality of VGAM129 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM129 RNA, herein designated VGAM RNA, and which when bound by VGAM129 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM129 host target proteins.

[1768] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM129 gene, herein designated VGAM GENE, on one or more VGAM129 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1769] It is yet further appreciated that a function of VGAM129 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM129 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM129 correlate with, and may be deduced from, the identity of the host target genes which VGAM129 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1770] Nucleotide sequences of the VGAM129 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM129 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM129 are further described hereinbelow with reference to Table 1.

[1771] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM129 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1772] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 130 (VGAM130) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1773] VGAM130 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM130 was detected is described hereinabove with reference to Figs. 2-8.

[1774] VGAM130 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM130 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1775] VGAM130 gene, herein designated VGAM GENE, encodes a VGAM130 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM130 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM130 precursor RNA is designated SEQ ID:2978, and is provided hereinbelow with reference to the sequence listing part.

[1776] VGAM130 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1777] An enzyme complex designated DICER COMPLEX, dices the VGAM130 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM130 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM130 RNA is designated SEQ ID:2979, and is provided hereinbelow with reference to the sequence listing part.

[1778] VGAM130 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1779] VGAM130 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM130 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1780] The complementary binding of VGAM130 RNA, herein designated VGAM RNA, to host target binding sites on VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM130 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM130 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1781] It is appreciated that VGAM130 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM130 host target genes. The mRNA of each one of this plurality of VGAM130 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM130 RNA, herein designated VGAM RNA, and which when bound by VGAM130 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM130 host target proteins.

[1782] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM130 gene, herein designated VGAM GENE, on one or more VGAM130 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1783] It is yet further appreciated that a function of VGAM130 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM130 correlate with, and may be deduced from, the identity of the host target genes which VGAM130 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1784] Nucleotide sequences of the VGAM130 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM130 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM130 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM130 are further described hereinbelow with reference to Table 1.

[1785] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM130 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1786] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 131 (VGAM131) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1787] VGAM131 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM131 was detected is described hereinabove with reference to Figs. 2-8.

[1788] VGAM131 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[1789] VGAM131 gene, herein designated VGAM GENE, encodes a VGAM131 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM131 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM131 precursor RNA is designated SEQ ID:2994, and is provided hereinbelow with reference to the sequence listing part.

[1790] VGAM131 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1791] An enzyme complex designated DICER COMPLEX, dices the VGAM131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM131 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM131 RNA is designated SEQ ID:2995, and is provided hereinbelow with reference to the sequence listing part.

[1792] VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1793] VGAM131 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM131 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM131 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1794] The complementary binding of VGAM131 RNA, herein designated VGAM RNA, to host target binding sites on VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM131 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1795] It is appreciated that VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM131 host target genes. The mRNA of each one of this plurality of VGAM131 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM131 RNA, herein designated VGAM RNA, and which when bound by VGAM131 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM131 host target proteins.

[1796] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM131 gene, herein designated VGAM GENE, on one or more VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1797] It is yet further appreciated that a function of VGAM131 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM131 correlate with, and may be deduced from, the identity of the host target genes which VGAM131 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1798] Nucleotide sequences of the VGAM131 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM131 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM131 are further de-

scribed hereinbelow with reference to Table 1.

[1799] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM131 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1800] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 132 (VGAM132) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1801] VGAM132 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM132 was detected is described hereinabove with reference to Figs. 2-8.

[1802] VGAM132 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM132 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1803] VGAM132 gene, herein designated VGAM GENE, encodes a VGAM132 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM132 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM132 precursor RNA is designated SEQ ID:2999, and is provided hereinbelow with reference to the sequence listing part.

[1804] VGAM132 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1805] An enzyme complex designated DICER COMPLEX, dices the VGAM132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM132 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM132 RNA is designated SEQ ID:3000, and is provided hereinbelow with reference to the sequence listing part.

[1806] VGAM132 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1807] VGAM132 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM132 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM132 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1808] The complementary binding of VGAM132 RNA, herein designated VGAM RNA, to host target binding sites on VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM132 host target protein, herein designated



VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1809] It is appreciated that VGAM132 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM132 host target genes. The mRNA of each one of this plurality of VGAM132 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM132 RNA, herein designated VGAM RNA, and which when bound by VGAM132 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM132 host target proteins.

[1810] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM132 gene, herein designated VGAM GENE, on one or more VGAM132 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1811] It is yet further appreciated that a function of VGAM132 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM132 correlate with, and may be deduced from, the identity of the host target genes which VGAM132 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1812] Nucleotide sequences of the VGAM132 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM132 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM132 are further described hereinbelow with reference to Table 1.

[1813] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM132 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1814] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 133 (VGAM133) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1815] VGAM133 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM133 was detected is described hereinabove with reference to Figs. 2-8.

[1816] VGAM133 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1817] VGAM133 gene, herein designated VGAM GENE, encodes a

VGAM133 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM133 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM133 precursor RNA is designated SEQ ID:3011, and is provided hereinbelow with reference to the sequence listing part.

[1818] VGAM133 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1819] An enzyme complex designated DICER COMPLEX, dices the VGAM133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM133 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM133 RNA is designated SEQ ID:3012, and is provided hereinbelow with reference to the sequence listing part.

[1820] VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1821] VGAM133 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM133 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1822] The complementary binding of VGAM133 RNA, herein designated VGAM RNA, to host target binding sites on VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM133 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[1823] It is appreciated that VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM133 host target genes. The mRNA of each one of this plurality of VGAM133 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM133 RNA, herein designated VGAM RNA, and which when bound by VGAM133 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM133 host target proteins.

[1824] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM133 gene, herein designated VGAM GENE, on one or more VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1825] It is yet further appreciated that a function of VGAM133 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM133 correlate with, and may be deduced from, the identity of the host target genes which VGAM133 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1826] Nucleotide sequences of the VGAM133 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM133 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM133 are further described hereinbelow with reference to Table 1.

[1827] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM133 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1828] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 134 (VGAM134) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1829] VGAM134 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM134 was detected is described hereinabove with reference to Figs. 2-8.

[1830] VGAM134 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1831] VGAM134 gene, herein designated VGAM GENE, encodes a VGAM134 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM134 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM134 precursor RNA is designated SEQ ID:3042, and is provided hereinbelow with reference to the sequence listing part.

[1832] VGAM134 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1833] An enzyme complex designated DICER COMPLEX, dices the VGAM134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM134 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM134 RNA is designated SEQ ID:2829, and is provided hereinbelow with reference to the sequence listing part.

[1834] VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1835] VGAM134 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM134 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1836] The complementary binding of VGAM134 RNA, herein designated VGAM RNA, to host target binding sites on VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM134 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1837] It is appreciated that VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM134 host target genes. The mRNA of each one of this plurality of VGAM134 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM134 RNA, herein designated VGAM RNA, and which when bound by VGAM134 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM134 host target proteins.

[1838] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM134 gene, herein designated VGAM GENE, on one or more VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1839] It is yet further appreciated that a function of VGAM134 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM134 correlate with, and may be deduced from, the identity of the host target genes which VGAM134 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1840] Nucleotide sequences of the VGAM134 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM134 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM134 are further described hereinbelow with reference to Table 1.

[1841] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM134 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1842] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 135 (VGAM135) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1843] VGAM135 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM135 was detected is described hereinabove with reference to Figs. 2–8.

[1844] VGAM135 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM135 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1845] VGAM135 gene, herein designated VGAM GENE, encodes a VGAM135 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM135 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM135 precursor RNA is designated SEQ ID:3043, and is provided hereinbelow with reference to the sequence listing part.

[1846] VGAM135 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1847] An enzyme complex designated DICER COMPLEX, dices the VGAM135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM135 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM135 RNA is designated SEQ ID:3044, and is provided hereinbelow with reference to the sequence listing part.

[1848] VGAM135 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1849] VGAM135 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM135 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1850] The complementary binding of VGAM135 RNA, herein designated VGAM RNA, to host target binding sites on VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM135 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1851] It is appreciated that VGAM135 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM135 host target genes. The mRNA of each one of this plurality of VGAM135 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM135 RNA, herein designated VGAM RNA, and which when bound by VGAM135 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM135 host target proteins.

[1852] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM135 gene, herein designated VGAM GENE, on one or more VGAM135 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1853] It is yet further appreciated that a function of VGAM135 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM135 correlate with, and may be deduced from, the identity of the host target genes which VGAM135 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1854] Nucleotide sequences of the VGAM135 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM135 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM135 are further described hereinbelow with reference to Table 1.

[1855] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM135 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1856] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 136 (VGAM136) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1857] VGAM136 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM136 was detected is described hereinabove with reference to Figs. 2–8.

[1858] VGAM136 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1859] VGAM136 gene, herein designated VGAM GENE, encodes a VGAM136 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM136 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM136 precursor RNA is designated SEQ ID:3051, and is provided hereinbelow with reference to the sequence listing part.

[1860] VGAM136 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1861] An enzyme complex designated DICER COMPLEX, dices the VGAM136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM136 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM136 RNA is designated SEQ ID:3052, and is provided hereinbelow with reference to the sequence listing part.

[1862] VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1863] VGAM136 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM136 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1864] The complementary binding of VGAM136 RNA, herein designated VGAM RNA, to host target binding sites on VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM136 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1865] It is appreciated that VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM136 host target genes. The mRNA of each one of this plurality of VGAM136 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM136 RNA, herein designated VGAM RNA, and which when bound by VGAM136 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM136 host target proteins.

[1866] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM136 gene, herein designated VGAM GENE, on one or more VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[1867] It is yet further appreciated that a function of VGAM136 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM136 correlate with, and may be deduced from, the identity of the host target genes which VGAM136 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1868] Nucleotide sequences of the VGAM136 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM136 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM136 are further described hereinbelow with reference to Table 1.

[1869] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM136 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1870] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 137 (VGAM137) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1871] VGAM137 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM137 was detected is described hereinabove with reference to Figs. 2–8.

[1872] VGAM137 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1873] VGAM137 gene, herein designated VGAM GENE, encodes a VGAM137 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM137 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM137 precursor RNA is designated SEQ ID:3062, and is provided hereinbelow with reference to the sequence listing part.

[1874] VGAM137 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1875] An enzyme complex designated DICER COMPLEX, dices the VGAM137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM137 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM137 RNA is designated SEQ ID:3063, and is provided hereinbelow with reference to the sequence listing part.

[1876] VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1877] VGAM137 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM137 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM137 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1878] The complementary binding of VGAM137 RNA, herein designated VGAM RNA, to host target binding sites on VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM137 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1879] It is appreciated that VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM137 host target genes. The mRNA of

each one of this plurality of VGAM137 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM137 RNA, herein designated VGAM RNA, and which when bound by VGAM137 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM137 host target proteins.

[1880] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM137 gene, herein designated VGAM GENE, on one or more VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[1881] It is yet further appreciated that a function of VGAM137 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM137 correlate with, and may be deduced from, the identity of the host target genes which VGAM137 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1882] Nucleotide sequences of the VGAM137 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM137 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM137 are further described hereinbelow with reference to Table 1.

[1883] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM137 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[1884] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 138 (VGAM138) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1885] VGAM138 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM138 was detected is described hereinabove with reference to Figs. 2–8.

[1886] VGAM138 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1887] VGAM138 gene, herein designated VGAM GENE, encodes a VGAM138 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM138 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM138 precursor RNA is designated SEQ ID:3067, and is provided hereinbelow with reference to the sequence listing part.

[1888] VGAM138 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1889] An enzyme complex designated DICER COMPLEX, dices the VGAM138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM138 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM138 RNA is designated SEQ ID:3068, and

is provided hereinbelow with reference to the sequence listing part.

[1890] VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1891] VGAM138 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM138 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM138 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1892] The complementary binding of VGAM138 RNA, herein designated VGAM RNA, to host target binding sites on VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM138 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1893] It is appreciated that VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM138 host target genes. The mRNA of each one of this plurality of VGAM138 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM138 RNA, herein designated VGAM RNA, and which when bound by VGAM138 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM138 host target proteins.

[1894] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM138 gene, herein designated VGAM GENE, on one or more VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1895] It is yet further appreciated that a function of VGAM138 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM138 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM138 correlate with, and may be deduced from, the identity of the host target genes which VGAM138 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1896] Nucleotide sequences of the VGAM138 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM138 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM138 are further described hereinbelow with reference to Table 1.

[1897] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM138 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1898] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 139 (VGAM139) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1899] VGAM139 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM139 was detected is described hereinabove with reference to Figs. 2–8.

[1900] VGAM139 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM139 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1901] VGAM139 gene, herein designated VGAM GENE, encodes a VGAM139 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM139 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM139 precursor RNA is

designated SEQ ID:3135, and is provided hereinbelow with reference to the sequence listing part.

[1902] VGAM139 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1903] An enzyme complex designated DICER COMPLEX, dices the VGAM139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM139 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM139 RNA is designated SEQ ID:2460, and is provided hereinbelow with reference to the sequence



listing part.

[1904] VGAM139 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1905] VGAM139 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM139 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM139 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1906] The complementary binding of VGAM139 RNA, herein designated VGAM RNA, to host target binding sites on VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM139 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1907] It is appreciated that VGAM139 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM139 host target genes. The mRNA of each one of this plurality of VGAM139 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM139 RNA, herein designated VGAM RNA, and which when bound by VGAM139 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM139 host target proteins.

[1908] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM139 gene, herein designated VGAM GENE, on one or more VGAM139 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1909] It is yet further appreciated that a function of VGAM139 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM139 correlate with, and may be deduced from, the identity of the host target genes which VGAM139 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1910] Nucleotide sequences of the VGAM139 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM139 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM139 are further described hereinbelow with reference to Table 1.

[1911] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM139 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1912] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 140 (VGAM140) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1913] VGAM140 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM140 was detected is described hereinabove with reference to Figs. 2–8.

[1914] VGAM140 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1915] VGAM140 gene, herein designated VGAM GENE, encodes a VGAM140 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM140 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM140 precursor RNA is designated SEQ ID:3136, and is provided hereinbelow with

reference to the sequence listing part.

[1916] VGAM140 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1917] An enzyme complex designated DICER COMPLEX, dices the VGAM140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM140 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM140 RNA is designated SEQ ID:3137, and is provided hereinbelow with reference to the sequence listing part.

[1918] VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1919] VGAM140 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM140 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1920] The complementary binding of VGAM140 RNA, herein designated VGAM RNA, to host target binding sites on VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM140 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1921] It is appreciated that VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM140 host target genes. The mRNA of each one of this plurality of VGAM140 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM140 RNA, herein designated VGAM RNA, and which when bound by VGAM140 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM140 host target proteins.

[1922] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM140 gene, herein designated VGAM GENE, on one or more VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1923] It is yet further appreciated that a function of VGAM140 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM140 correlate with, and may be deduced from, the identity of the host target genes which VGAM140 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1924] Nucleotide sequences of the VGAM140 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM140 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM140 are further described hereinbelow with reference to Table 1.

[1925] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM140 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1926] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 141 (VGAM141) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1927] VGAM141 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM141 was detected is described hereinabove with reference to Figs. 2–8.

[1928] VGAM141 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM141 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1929] VGAM141 gene, herein designated VGAM GENE, encodes a VGAM141 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM141 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM141 precursor RNA is designated SEQ ID:3175, and is provided hereinbelow with reference to the sequence listing part.

[1930] VGAM141 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1931] An enzyme complex designated DICER COMPLEX, dices the VGAM141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM141 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM141 RNA is designated SEQ ID:3176, and is provided hereinbelow with reference to the sequence listing part.

[1932] VGAM141 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1933] VGAM141 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM141 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM141 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1934] The complementary binding of VGAM141 RNA, herein designated VGAM RNA, to host target binding sites on VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM141 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1935] It is appreciated that VGAM141 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM141 host target genes. The mRNA of each one of this plurality of VGAM141 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM141 RNA, herein designated VGAM

RNA, and which when bound by VGAM141 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM141 host target proteins.

[1936] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM141 gene, herein designated VGAM GENE, on one or more VGAM141 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1937] It is yet further appreciated that a function of VGAM141 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM141 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM141 correlate with, and may be deduced from, the identity of the host target genes which VGAM141 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1938] Nucleotide sequences of the VGAM141 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM141 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM141 are further described hereinbelow with reference to Table 1.

[1939] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM141 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1940] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 142 (VGAM142) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1941] VGAM142 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM142 was detected is described hereinabove with reference to Figs. 2–8.

[1942] VGAM142 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM142 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1943] VGAM142 gene, herein designated VGAM GENE, encodes a VGAM142 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM142 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM142 precursor RNA is designated SEQ ID:3183, and is provided hereinbelow with reference to the sequence listing part.

[1944] VGAM142 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1945] An enzyme complex designated DICER COMPLEX, dices the VGAM142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM142 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM142 RNA is designated SEQ ID:3184, and is provided hereinbelow with reference to the sequence listing part.

[1946] VGAM142 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1947] VGAM142 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM142 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM142 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1948] The complementary binding of VGAM142 RNA, herein designated VGAM RNA, to host target binding sites on VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM142 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1949] It is appreciated that VGAM142 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM142 host target genes. The mRNA of each one of this plurality of VGAM142 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM142 RNA, herein designated VGAM RNA, and which when bound by VGAM142 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM142 host target proteins.

[1950] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM142 gene, herein designated VGAM GENE, on one or more VGAM142 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1951] It is yet further appreciated that a function of VGAM142 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM142 include diagnosis, prevention and

treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM142 correlate with, and may be deduced from, the identity of the host target genes which VGAM142 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1952] Nucleotide sequences of the VGAM142 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM142 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM142 are further described hereinbelow with reference to Table 1.

[1953] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM142 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1954] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 143 (VGAM143) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[1955] VGAM143 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM143 was detected is described hereinabove with reference to Figs. 2–8.

[1956] VGAM143 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM143 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1957] VGAM143 gene, herein designated VGAM GENE, encodes a VGAM143 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM143 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM143 precursor RNA is designated SEQ ID:3212, and is provided hereinbelow with reference to the sequence listing part.

[1958] VGAM143 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM143 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1959] An enzyme complex designated DICER COMPLEX, dices the VGAM143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM143 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM143 RNA is designated SEQ ID:3213, and is provided hereinbelow with reference to the sequence listing part.

[1960] VGAM143 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM143 host target RNA, herein designated VGAM



HOST TARGET RNA. VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1961] VGAM143 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM143 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM143 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1962] The complementary binding of VGAM143 RNA, herein designated VGAM RNA, to host target binding sites on VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM143 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1963] It is appreciated that VGAM143 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM143 host target genes. The mRNA of each one of this plurality of VGAM143 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM143 RNA, herein designated VGAM RNA, and which when bound by VGAM143 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM143 host target proteins.

[1964] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM143 gene, herein designated VGAM GENE, on one or more VGAM143 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1965] It is yet further appreciated that a function of VGAM143 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM143 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B.

Specific functions, and accordingly utilities, of VGAM143 correlate with, and may be deduced from, the identity of the host target genes which VGAM143 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1966] Nucleotide sequences of the VGAM143 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM143 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM143 are further described hereinbelow with reference to Table 1.

[1967] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM143 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1968] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 144 (VGAM144) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[1969] VGAM144 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM144 was detected is described hereinabove with reference to Figs. 2–8.

[1970] VGAM144 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM144 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1971] VGAM144 gene, herein designated VGAM GENE, encodes a VGAM144 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM144 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM144 precursor RNA is designated SEQ ID:3218, and is provided hereinbelow with reference to the sequence listing part.

[1972] VGAM144 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM144 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1973] An enzyme complex designated DICER COMPLEX, dices the VGAM144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM144 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM144 RNA is designated SEQ ID:3219, and is provided hereinbelow with reference to the sequence listing part.

[1974] VGAM144 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM144 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1975] VGAM144 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM144 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1976] The complementary binding of VGAM144 RNA, herein designated VGAM RNA, to host target binding sites on VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM144 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1977] It is appreciated that VGAM144 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM144 host target genes. The mRNA of each one of this plurality of VGAM144 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM144 RNA, herein designated VGAM RNA, and which when bound by VGAM144 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM144 host target proteins.



[1978] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM144 gene, herein designated VGAM GENE, on one or more VGAM144 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1979] It is yet further appreciated that a function of VGAM144 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM144

correlate with, and may be deduced from, the identity of the host target genes which VGAM144 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1980] Nucleotide sequences of the VGAM144 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM144 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM144 are further described hereinbelow with reference to Table 1.

[1981] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM144 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1982] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 145 (VGAM145) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[1983] VGAM145 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM145 was detected is described hereinabove with reference to Figs. 2–8.

[1984] VGAM145 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM145 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1985] VGAM145 gene, herein designated VGAM GENE, encodes a VGAM145 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM145 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM145 precursor RNA is designated SEQ ID:3235, and is provided hereinbelow with reference to the sequence listing part.

[1986] VGAM145 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[1987] An enzyme complex designated DICER COMPLEX, dices the VGAM145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM145 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM145 RNA is designated SEQ ID:3236, and is provided hereinbelow with reference to the sequence listing part.

[1988] VGAM145 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[1989] VGAM145 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM145 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM145 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[1990] The complementary binding of VGAM145 RNA, herein designated VGAM RNA, to host target binding sites on VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM145 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[1991] It is appreciated that VGAM145 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM145 host target genes. The mRNA of each one of this plurality of VGAM145 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM145 RNA, herein designated VGAM RNA, and which when bound by VGAM145 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM145 host target proteins.

[1992] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM145 gene, herein designated VGAM GENE, on one or more VGAM145 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[1993] It is yet further appreciated that a function of VGAM145 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM145 include diagnosis, prevention and treatment of viral infection by Macaca mulatta rhadinovirus. Specific functions, and accordingly utilities, of VGAM145 correlate with, and may be deduced from, the

identity of the host target genes which VGAM145 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[1994] Nucleotide sequences of the VGAM145 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM145 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM145 are further described hereinbelow with reference to Table 1.

[1995] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM145 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[1996] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 146 (VGAM146) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[1997] VGAM146 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM146 was detected is described hereinabove with reference to Figs. 2–8.

[1998] VGAM146 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM146 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[1999] VGAM146 gene, herein designated VGAM GENE, encodes a VGAM146 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM146 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM146 precursor RNA is designated SEQ ID:3240, and is provided hereinbelow with reference to the sequence listing part.

[2000] VGAM146 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2001] An enzyme complex designated DICER COMPLEX, dices the VGAM146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM146 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM146 RNA is designated SEQ ID:3241, and is provided hereinbelow with reference to the sequence listing part.

[2002] VGAM146 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2003] VGAM146 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM146 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2004] The complementary binding of VGAM146 RNA, herein designated VGAM RNA, to host target binding sites on VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM146 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2005] It is appreciated that VGAM146 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM146 host target genes. The mRNA of each one of this plurality of VGAM146 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM146 RNA, herein designated VGAM RNA, and which when bound by VGAM146 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM146 host target proteins.

[2006] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM146 gene, herein designated VGAM GENE, on one or more VGAM146 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2007] It is yet further appreciated that a function of VGAM146 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM146 correlate with, and may be deduced from, the identity of the host target genes which VGAM146 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[2008] Nucleotide sequences of the VGAM146 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM146 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM146 are further described hereinbelow with reference to Table 1.

[2009] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM146 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2010] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 147 (VGAM147) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2011] VGAM147 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM147 was detected is described hereinabove with reference to Figs. 2–8.

[2012] VGAM147 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM147 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2013] VGAM147 gene, herein designated VGAM GENE, encodes a VGAM147 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM147 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM147 precursor RNA is designated SEQ ID:3261, and is provided hereinbelow with reference to the sequence listing part.

[2014] VGAM147 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2015] An enzyme complex designated DICER COMPLEX, dices the VGAM147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM147 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM147 RNA is designated SEQ ID:3262, and is provided hereinbelow with reference to the sequence listing part.

[2016] VGAM147 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2017] VGAM147 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM147 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[2018] The complementary binding of VGAM147 RNA, herein designated VGAM RNA, to host target binding sites on VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM147 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2019] It is appreciated that VGAM147 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM147 host target genes. The mRNA of each one of this plurality of VGAM147 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM147 RNA, herein designated VGAM RNA, and which when bound by VGAM147 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM147 host target proteins.

[2020] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM147 gene, herein designated VGAM GENE, on one or more VGAM147 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2021] It is yet further appreciated that a function of VGAM147 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM147 correlate with, and may be deduced from, the identity of the host target genes which VGAM147 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[2022] Nucleotide sequences of the VGAM147 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM147 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM147 are further described hereinbelow with reference to Table 1.

[2023] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM147 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2024] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 148 (VGAM148) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2025] VGAM148 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM148 was detected is described hereinabove with reference to Figs. 2–8.

[2026] VGAM148 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2027] VGAM148 gene, herein designated VGAM GENE, encodes a VGAM148 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM148 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM148 precursor RNA is designated SEQ ID:3268, and is provided hereinbelow with reference to the sequence listing part.

[2028] VGAM148 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2029] An enzyme complex designated DICER COMPLEX, dices the VGAM148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM148 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM148 RNA is designated SEQ ID:3269, and is provided hereinbelow with reference to the sequence listing part.

[2030] VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[2031] VGAM148 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM148 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2032] The complementary binding of VGAM148 RNA, herein designated VGAM RNA, to host target binding sites on VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM148 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2033] It is appreciated that VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM148 host target genes. The mRNA of each one of this plurality of VGAM148 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM148 RNA, herein designated VGAM RNA, and which when bound by VGAM148 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM148 host target proteins.

[2034] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM148 gene, herein designated VGAM GENE, on one or



more VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2035] It is yet further appreciated that a function of VGAM148 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM148 correlate with, and may be deduced from, the identity of the host target genes which VGAM148 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2036] Nucleotide sequences of the VGAM148 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM148 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM148 are further described hereinbelow with reference to Table 1.

[2037] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM148 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2038] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 149 (VGAM149) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2039] VGAM149 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM149 was detected is described

hereinabove with reference to Figs. 2–8.

[2040] VGAM149 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM149 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2041] VGAM149 gene, herein designated VGAM GENE, encodes a VGAM149 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM149 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM149 precursor RNA is designated SEQ ID:3278, and is provided hereinbelow with reference to the sequence listing part.

[2042] VGAM149 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2043] An enzyme complex designated DICER COMPLEX, dices the VGAM149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM149 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM149 RNA is designated SEQ ID:3279, and is provided hereinbelow with reference to the sequence listing part.

[2044] VGAM149 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2045] VGAM149 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM149 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM149 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2046] The complementary binding of VGAM149 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM149 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2047] It is appreciated that VGAM149 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM149 host target genes. The mRNA of each one of this plurality of VGAM149 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM149 RNA, herein designated VGAM RNA, and which when bound by VGAM149 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM149 host target proteins.

[2048] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM149 gene, herein designated VGAM GENE, on one or more VGAM149 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2049] It is yet further appreciated that a function of VGAM149 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM149 correlate with, and may be deduced from, the identity of the host target genes which VGAM149 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2050] Nucleotide sequences of the VGAM149 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM149 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM149 are further described hereinbelow with reference to Table 1.

[2051] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM149 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2052] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 150 (VGAM150) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2053] VGAM150 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM150 was detected is described hereinabove with reference to Figs. 2-8.



[2054] VGAM150 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2055] VGAM150 gene, herein designated VGAM GENE, encodes a VGAM150 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM150 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM150 precursor RNA is designated SEQ ID:3287, and is provided hereinbelow with reference to the sequence listing part.

[2056] VGAM150 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[2057] An enzyme complex designated DICER COMPLEX, dices the VGAM150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM150 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM150 RNA is designated SEQ ID:3288, and is provided hereinbelow with reference to the sequence listing part.

[2058] VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2059] VGAM150 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM150 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM150 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2060] The complementary binding of VGAM150 RNA, herein designated VGAM RNA, to host target binding sites on VGAM150 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM150 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2061] It is appreciated that VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM150 host target genes. The mRNA of each one of this plurality of VGAM150 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM150 RNA, herein designated VGAM RNA, and which when bound by VGAM150 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM150 host target proteins.

[2062] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM150 gene, herein designated VGAM GENE, on one or more VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2063] It is yet further appreciated that a function of VGAM150 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM150 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM150 correlate with, and may be deduced from, the identity of the host target genes which VGAM150 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2064] Nucleotide sequences of the VGAM150 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM150 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM150 are further described hereinbelow with reference to Table 1.

[2065] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM150 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2066] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 151 (VGAM151) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2067] VGAM151 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM151 was detected is described hereinabove with reference to Figs. 2-8.

[2068] VGAM151 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Macaca mulatta rhadi-*

novirus. VGAM151 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2069] VGAM151 gene, herein designated VGAM GENE, encodes a VGAM151 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM151 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM151 precursor RNA is designated SEQ ID:3311, and is provided hereinbelow with reference to the sequence listing part.

[2070] VGAM151 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2071] An enzyme complex designated DICER COMPLEX, dices



the VGAM151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM151 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM151 RNA is designated SEQ ID:3312, and is provided hereinbelow with reference to the sequence listing part.

[2072] VGAM151 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2073] VGAM151 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM151 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM151 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM151 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2074] The complementary binding of VGAM151 RNA, herein designated VGAM RNA, to host target binding sites on VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM151 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2075] It is appreciated that VGAM151 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM151 host target genes. The mRNA of each one of this plurality of VGAM151 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM151 RNA, herein designated VGAM RNA, and which when bound by VGAM151 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM151 host target proteins.

[2076] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM151 gene, herein designated VGAM GENE, on one or more VGAM151 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2077] It is yet further appreciated that a function of VGAM151 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM151 correlate with, and may be deduced from, the identity of the host target genes which VGAM151 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2078] Nucleotide sequences of the VGAM151 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM151 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM151 are further described hereinbelow with reference to Table 1.

[2079] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM151 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2080] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 152 (VGAM152) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2081] VGAM152 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM152 was detected is described hereinabove with reference to Figs. 2-8.

[2082] VGAM152 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM152 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2083] VGAM152 gene, herein designated VGAM GENE, encodes a VGAM152 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM152 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM152 precursor RNA is designated SEQ ID:3319, and is provided hereinbelow with reference to the sequence listing part.

[2084] VGAM152 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2085] An enzyme complex designated DICER COMPLEX, dices the VGAM152 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM152 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM152 RNA is designated SEQ ID:3320, and is provided hereinbelow with reference to the sequence listing part.

[2086] VGAM152 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2087] VGAM152 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM152 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2088] The complementary binding of VGAM152 RNA, herein designated VGAM RNA, to host target binding sites on VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM152 host tar-



get RNA, herein designated VGAM HOST TARGET RNA, into VGAM152 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2089] It is appreciated that VGAM152 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM152 host target genes. The mRNA of each one of this plurality of VGAM152 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM152 RNA, herein designated VGAM RNA, and which when bound by VGAM152 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM152 host target proteins.

[2090] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM152 gene, herein designated VGAM GENE, on one or more VGAM152 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2091] It is yet further appreciated that a function of VGAM152 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM152 correlate with, and may be deduced from, the identity of the host target genes which VGAM152 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2092] Nucleotide sequences of the VGAM152 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM152 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM152 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM152 are further described hereinbelow with reference to Table 1.

[2093] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM152 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2094] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 153 (VGAM153) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2095] VGAM153 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM153 was detected is described hereinabove with reference to Figs. 2-8.

[2096] VGAM153 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[2097] VGAM153 gene, herein designated VGAM GENE, encodes a VGAM153 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM153 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM153 precursor RNA is designated SEQ ID:3338, and is provided hereinbelow with reference to the sequence listing part.

[2098] VGAM153 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2099] An enzyme complex designated DICER COMPLEX, dices the VGAM153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM153 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM153 RNA is designated SEQ ID:3339, and is provided hereinbelow with reference to the sequence listing part.

[2100] VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2101] VGAM153 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM153 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM153 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2102] The complementary binding of VGAM153 RNA, herein designated VGAM RNA, to host target binding sites on VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM153 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2103] It is appreciated that VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM153 host target genes. The mRNA of each one of this plurality of VGAM153 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM153 RNA, herein designated VGAM RNA, and which when bound by VGAM153 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM153 host target proteins.

[2104] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM153 gene, herein designated VGAM GENE, on one or more VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2105] It is yet further appreciated that a function of VGAM153 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM153 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM153 correlate with, and may be deduced from, the identity of the host target genes which VGAM153 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2106] Nucleotide sequences of the VGAM153 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM153 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM153 are further de-



scribed hereinbelow with reference to Table 1.

[2107] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM153 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2108] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 154 (VGAM154) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2109] VGAM154 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM154 was detected is described hereinabove with reference to Figs. 2-8.

[2110] VGAM154 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2111] VGAM154 gene, herein designated VGAM GENE, encodes a VGAM154 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM154 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM154 precursor RNA is designated SEQ ID:3359, and is provided hereinbelow with reference to the sequence listing part.

[2112] VGAM154 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2113] An enzyme complex designated DICER COMPLEX, dices the VGAM154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM154 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM154 RNA is designated SEQ ID:3360, and is provided hereinbelow with reference to the sequence listing part.

[2114] VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2115] VGAM154 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM154 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM154 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2116] The complementary binding of VGAM154 RNA, herein designated VGAM RNA, to host target binding sites on VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM154 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2117] It is appreciated that VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM154 host target genes. The mRNA of each one of this plurality of VGAM154 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM154 RNA, herein designated VGAM RNA, and which when bound by VGAM154 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM154 host target proteins.

[2118] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM154 gene, herein designated VGAM GENE, on one or more VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2119] It is yet further appreciated that a function of VGAM154 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM154 correlate with, and may be deduced from, the identity of the host target genes which VGAM154 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2120] Nucleotide sequences of the VGAM154 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM154 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM154 are further described hereinbelow with reference to Table 1.

[2121] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM154 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2122] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 155 (VGAM155) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2123] VGAM155 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM155 was detected is described hereinabove with reference to Figs. 2-8.

[2124] VGAM155 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM155 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2125] VGAM155 gene, herein designated VGAM GENE, encodes a

VGAM155 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM155 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM155 precursor RNA is designated SEQ ID:3375, and is provided hereinbelow with reference to the sequence listing part.

[2126] VGAM155 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2127] An enzyme complex designated DICER COMPLEX, dices the VGAM155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM155 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM155 RNA is designated SEQ ID:3376, and is provided hereinbelow with reference to the sequence listing part.

[2128] VGAM155 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2129] VGAM155 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM155 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM155 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2130] The complementary binding of VGAM155 RNA, herein designated VGAM RNA, to host target binding sites on VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM155 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[2131] It is appreciated that VGAM155 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM155 host target genes. The mRNA of each one of this plurality of VGAM155 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM155 RNA, herein designated VGAM RNA, and which when bound by VGAM155 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM155 host target proteins.

[2132] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM155 gene, herein designated VGAM GENE, on one or more VGAM155 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2133] It is yet further appreciated that a function of VGAM155 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM155 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM155 correlate with, and may be deduced from, the identity of the host target genes which VGAM155 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2134] Nucleotide sequences of the VGAM155 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM155 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM155 are further described hereinbelow with reference to Table 1.

[2135] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM155 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2136] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 156 (VGAM156) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2137] VGAM156 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM156 was detected is described hereinabove with reference to Figs. 2-8.

[2138] VGAM156 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus. VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2139] VGAM156 gene, herein designated VGAM GENE, encodes a VGAM156 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM156 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM156 precursor RNA is designated SEQ ID:3406, and is provided hereinbelow with reference to the sequence listing part.

[2140] VGAM156 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2141] An enzyme complex designated DICER COMPLEX, dices the VGAM156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM156 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM156 RNA is designated SEQ ID:3407, and is provided hereinbelow with reference to the sequence listing part.

[2142] VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2143] VGAM156 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM156 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM156 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2144] The complementary binding of VGAM156 RNA, herein designated VGAM RNA, to host target binding sites on VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM156 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[2145] It is appreciated that VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM156 host target genes. The mRNA of each one of this plurality of VGAM156 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM156 RNA, herein designated VGAM RNA, and which when bound by VGAM156 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM156 host target proteins.

[2146] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM156 gene, herein designated VGAM GENE, on one or more VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2147] It is yet further appreciated that a function of VGAM156 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM156 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus. Specific functions, and accordingly utilities, of VGAM156 correlate with, and may be deduced from, the identity of the host target genes which VGAM156 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2148] Nucleotide sequences of the VGAM156 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM156 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM156 are further described hereinbelow with reference to Table 1.

[2149] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM156 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2150] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 157 (VGAM157) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2151] VGAM157 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM157 was detected is described hereinabove with reference to Figs. 2–8.

[2152] VGAM157 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM157 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2153] VGAM157 gene, herein designated VGAM GENE, encodes a VGAM157 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM157 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM157 precursor RNA is designated SEQ ID:3499, and is provided hereinbelow with reference to the sequence listing part.

[2154] VGAM157 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2155] An enzyme complex designated DICER COMPLEX, dices the VGAM157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM157 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM157 RNA is designated SEQ ID:3500, and is provided hereinbelow with reference to the sequence listing part.

[2156] VGAM157 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2157] VGAM157 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM157 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2158] The complementary binding of VGAM157 RNA, herein designated VGAM RNA, to host target binding sites on VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM157 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2159] It is appreciated that VGAM157 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM157 host target genes. The mRNA of each one of this plurality of VGAM157 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM157 RNA, herein designated VGAM RNA, and which when bound by VGAM157 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM157 host target proteins.

[2160] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM157 gene, herein designated VGAM GENE, on one or more VGAM157 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2161] It is yet further appreciated that a function of VGAM157 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM157 correlate with, and may be deduced from, the identity of the host target genes which VGAM157 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2162] Nucleotide sequences of the VGAM157 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM157 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM157 are further described hereinbelow with reference to Table 1.

[2163] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the



complementarity of each of these host target binding sites to VGAM157 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2164] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 158 (VGAM158) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2165] VGAM158 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM158 was detected is described hereinabove with reference to Figs. 2–8.

[2166] VGAM158 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM158 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2167] VGAM158 gene, herein designated VGAM GENE, encodes a VGAM158 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM158 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM158 precursor RNA is designated SEQ ID:3509, and is provided hereinbelow with reference to the sequence listing part.

[2168] VGAM158 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2169] An enzyme complex designated DICER COMPLEX, dices the VGAM158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM158 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM158 RNA is designated SEQ ID:3510, and is provided hereinbelow with reference to the sequence listing part.

[2170] VGAM158 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2171] VGAM158 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM158 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM158 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2172] The complementary binding of VGAM158 RNA, herein designated VGAM RNA, to host target binding sites on VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM158 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2173] It is appreciated that VGAM158 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM158 host target genes. The mRNA of each one of this plurality of VGAM158 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM158 RNA, herein designated VGAM RNA, and which when bound by VGAM158 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM158 host target proteins.

[2174] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM158 gene, herein designated VGAM GENE, on one or more VGAM158 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [2175] It is yet further appreciated that a function of VGAM158 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM158 correlate with, and may be deduced from, the identity of the host target genes which VGAM158 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [2176] Nucleotide sequences of the VGAM158 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM158 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM158 are further described hereinbelow with reference to Table 1.
- [2177] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM158 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2178] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 159 (VGAM159) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2179] VGAM159 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM159 was detected is described hereinabove with reference to Figs. 2–8.

[2180] VGAM159 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2181] VGAM159 gene, herein designated VGAM GENE, encodes a VGAM159 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM159 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM159 precursor RNA is designated SEQ ID:3550, and is provided hereinbelow with reference to the sequence listing part.

[2182] VGAM159 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2183] An enzyme complex designated DICER COMPLEX, dices the VGAM159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM159 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-



quence of VGAM159 RNA is designated SEQ ID:3551, and is provided hereinbelow with reference to the sequence listing part.

[2184] VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2185] VGAM159 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM159 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2186] The complementary binding of VGAM159 RNA, herein designated VGAM RNA, to host target binding sites on VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM159 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2187] It is appreciated that VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM159 host target genes. The mRNA of

each one of this plurality of VGAM159 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM159 RNA, herein designated VGAM RNA, and which when bound by VGAM159 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM159 host target proteins.

[2188] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM159 gene, herein designated VGAM GENE, on one or more VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[2189] It is yet further appreciated that a function of VGAM159 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM159 correlate with, and may be deduced from, the identity of the host target genes which VGAM159 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2190] Nucleotide sequences of the VGAM159 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM159 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM159 are further described hereinbelow with reference to Table 1.

[2191] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM159 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[2192] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 160 (VGAM160) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2193] VGAM160 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM160 was detected is described hereinabove with reference to Figs. 2–8.

[2194] VGAM160 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM160 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2195] VGAM160 gene, herein designated VGAM GENE, encodes a VGAM160 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM160 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM160 precursor RNA is designated SEQ ID:3564, and is provided hereinbelow with reference to the sequence listing part.

[2196] VGAM160 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2197] An enzyme complex designated DICER COMPLEX, dices the VGAM160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM160 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM160 RNA is designated SEQ ID:3565, and

is provided hereinbelow with reference to the sequence listing part.

[2198] VGAM160 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2199] VGAM160 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM160 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM160 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2200] The complementary binding of VGAM160 RNA, herein designated VGAM RNA, to host target binding sites on VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM160 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2201] It is appreciated that VGAM160 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM160 host target genes. The mRNA of each one of this plurality of VGAM160 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM160 RNA, herein designated VGAM RNA, and which when bound by VGAM160 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM160 host target proteins.

[2202] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM160 gene, herein designated VGAM GENE, on one or more VGAM160 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2203] It is yet further appreciated that a function of VGAM160 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM160 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM160 correlate with, and may be deduced from, the identity of the host target genes which VGAM160 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2204] Nucleotide sequences of the VGAM160 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM160 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM160 are further described hereinbelow with reference to Table 1.

[2205] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM160 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2206] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 161 (VGAM161) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2207] VGAM161 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM161 was detected is described hereinabove with reference to Figs. 2–8.

[2208] VGAM161 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2209] VGAM161 gene, herein designated VGAM GENE, encodes a VGAM161 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM161 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM161 precursor RNA is

designated SEQ ID:3572, and is provided hereinbelow with reference to the sequence listing part.

[2210] VGAM161 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2211] An enzyme complex designated DICER COMPLEX, dices the VGAM161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM161 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM161 RNA is designated SEQ ID:3573, and is provided hereinbelow with reference to the sequence

listing part.

[2212] VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2213] VGAM161 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM161 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM161 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2214] The complementary binding of VGAM161 RNA, herein designated VGAM RNA, to host target binding sites on VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM161 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2215] It is appreciated that VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM161 host target genes. The mRNA of each one of this plurality of VGAM161 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM161 RNA, herein designated VGAM RNA, and which when bound by VGAM161 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM161 host target proteins.

[2216] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM161 gene, herein designated VGAM GENE, on one or more VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2217] It is yet further appreciated that a function of VGAM161 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM161 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM161 correlate with, and may be deduced from, the identity of the host target genes which VGAM161 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2218] Nucleotide sequences of the VGAM161 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM161 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM161 are further described hereinbelow with reference to Table 1.

[2219] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM161 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2220] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 162 (VGAM162) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2221] VGAM162 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM162 was detected is described hereinabove with reference to Figs. 2–8.

[2222] VGAM162 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM162 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2223] VGAM162 gene, herein designated VGAM GENE, encodes a VGAM162 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM162 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM162 precursor RNA is designated SEQ ID:3582, and is provided hereinbelow with

reference to the sequence listing part.

[2224] VGAM162 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2225] An enzyme complex designated DICER COMPLEX, dices the VGAM162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM162 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM162 RNA is designated SEQ ID:3583, and is provided hereinbelow with reference to the sequence listing part.

[2226] VGAM162 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2227] VGAM162 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM162 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2228] The complementary binding of VGAM162 RNA, herein designated VGAM RNA, to host target binding sites on VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM162 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2229] It is appreciated that VGAM162 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM162 host target genes. The mRNA of each one of this plurality of VGAM162 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM162 RNA, herein designated VGAM RNA, and which when bound by VGAM162 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM162 host target proteins.

[2230] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM162 gene, herein designated VGAM GENE, on one or more VGAM162 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2231] It is yet further appreciated that a function of VGAM162 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM162 correlate with, and may be deduced from, the identity of the host target genes which VGAM162 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2232] Nucleotide sequences of the VGAM162 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM162 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM162 are further described hereinbelow with reference to Table 1.

[2233] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM162 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2234] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 163 (VGAM163) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2235] VGAM163 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM163 was detected is described hereinabove with reference to Figs. 2–8.

[2236] VGAM163 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM163 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2237] VGAM163 gene, herein designated VGAM GENE, encodes a VGAM163 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM163 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM163 precursor RNA is designated SEQ ID:3610, and is provided hereinbelow with reference to the sequence listing part.

[2238] VGAM163 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2239] An enzyme complex designated DICER COMPLEX, dices the VGAM163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM163 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM163 RNA is designated SEQ ID:3611, and is provided hereinbelow with reference to the sequence listing part.

[2240] VGAM163 host target gene, herein designated VGAM



HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2241] VGAM163 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM163 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM163 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2242] The complementary binding of VGAM163 RNA, herein designated VGAM RNA, to host target binding sites on VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM163 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2243] It is appreciated that VGAM163 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM163 host target genes. The mRNA of each one of this plurality of VGAM163 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM163 RNA, herein designated VGAM

RNA, and which when bound by VGAM163 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM163 host target proteins.

[2244] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM163 gene, herein designated VGAM GENE, on one or more VGAM163 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2245] It is yet further appreciated that a function of VGAM163 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM163 include diagnosis, prevention and treatment of viral infection by Mollusum contagiosum virus. Specific functions, and accordingly utilities, of VGAM163 correlate with, and may be deduced from, the identity of the host target genes which VGAM163 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2246] Nucleotide sequences of the VGAM163 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM163 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM163 are further described hereinbelow with reference to Table 1.

[2247] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM163 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2248] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 164 (VGAM164) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2249] VGAM164 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM164 was detected is described hereinabove with reference to Figs. 2–8.

[2250] VGAM164 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2251] VGAM164 gene, herein designated VGAM GENE, encodes a VGAM164 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM164 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM164 precursor RNA is designated SEQ ID:3619, and is provided hereinbelow with reference to the sequence listing part.

[2252] VGAM164 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2253] An enzyme complex designated DICER COMPLEX, dices the VGAM164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM164 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM164 RNA is designated SEQ ID:3620, and is provided hereinbelow with reference to the sequence listing part.

[2254] VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2255] VGAM164 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM164 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM164 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM164 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2256] The complementary binding of VGAM164 RNA, herein designated VGAM RNA, to host target binding sites on VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM164 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2257] It is appreciated that VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM164 host target genes. The mRNA of each one of this plurality of VGAM164 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM164 RNA, herein designated VGAM RNA, and which when bound by VGAM164 RNA, herein



designated VGAM RNA, causes inhibition of translation of respective one or more VGAM164 host target proteins.

[2258] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM164 gene, herein designated VGAM GENE, on one or more VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2259] It is yet further appreciated that a function of VGAM164 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM164 include diagnosis, prevention and

treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM164 correlate with, and may be deduced from, the identity of the host target genes which VGAM164 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2260] Nucleotide sequences of the VGAM164 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM164 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM164 are further described hereinbelow with reference to Table 1.

[2261] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM164 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2262] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 165 (VGAM165) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2263] VGAM165 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM165 was detected is described hereinabove with reference to Figs. 2–8.

[2264] VGAM165 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2265] VGAM165 gene, herein designated VGAM GENE, encodes a VGAM165 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM165 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM165 precursor RNA is designated SEQ ID:3632, and is provided hereinbelow with reference to the sequence listing part.

[2266] VGAM165 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM165 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2267] An enzyme complex designated DICER COMPLEX, dices the VGAM165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM165 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM165 RNA is designated SEQ ID:3633, and is provided hereinbelow with reference to the sequence listing part.

[2268] VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM165 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2269] VGAM165 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM165 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2270] The complementary binding of VGAM165 RNA, herein designated VGAM RNA, to host target binding sites on VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM165 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2271] It is appreciated that VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM165 host target genes. The mRNA of each one of this plurality of VGAM165 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM165 RNA, herein designated VGAM RNA, and which when bound by VGAM165 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM165 host target proteins.

[2272] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM165 gene, herein designated VGAM GENE, on one or more VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2273] It is yet further appreciated that a function of VGAM165 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1.

Specific functions, and accordingly utilities, of VGAM165 correlate with, and may be deduced from, the identity of the host target genes which VGAM165 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2274] Nucleotide sequences of the VGAM165 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM165 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM165 are further described hereinbelow with reference to Table 1.

[2275] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM165 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2276] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 166 (VGAM166) viral gene, which modulates expression of respective host target genes thereof, the func-



tion and utility of which host target genes is known in the art.

[2277] VGAM166 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM166 was detected is described hereinabove with reference to Figs. 2–8.

[2278] VGAM166 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2279] VGAM166 gene, herein designated VGAM GENE, encodes a VGAM166 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM166 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM166 precursor RNA is designated SEQ ID:3662, and is provided hereinbelow with reference to the sequence listing part.

[2280] VGAM166 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM166 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2281] An enzyme complex designated DICER COMPLEX, dices the VGAM166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM166 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM166 RNA is designated SEQ ID:3663, and is provided hereinbelow with reference to the sequence listing part.

[2282] VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM166 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2283] VGAM166 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM166 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2284] The complementary binding of VGAM166 RNA, herein designated VGAM RNA, to host target binding sites on VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM166 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2285] It is appreciated that VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM166 host target genes. The mRNA of each one of this plurality of VGAM166 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM166 RNA, herein designated VGAM RNA, and which when bound by VGAM166 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM166 host target proteins.

[2286] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM166 gene, herein designated VGAM GENE, on one or more VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2287] It is yet further appreciated that a function of VGAM166 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM166

correlate with, and may be deduced from, the identity of the host target genes which VGAM166 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2288] Nucleotide sequences of the VGAM166 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM166 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM166 are further described hereinbelow with reference to Table 1.

[2289] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM166 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2290] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 167 (VGAM167) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[2291] VGAM167 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM167 was detected is described hereinabove with reference to Figs. 2–8.

[2292] VGAM167 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2293] VGAM167 gene, herein designated VGAM GENE, encodes a VGAM167 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM167 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM167 precursor RNA is designated SEQ ID:3670, and is provided hereinbelow with reference to the sequence listing part.

[2294] VGAM167 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2295] An enzyme complex designated DICER COMPLEX, dices the VGAM167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM167 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM167 RNA is designated SEQ ID:3671, and is provided hereinbelow with reference to the sequence listing part.

[2296] VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-



gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2297] VGAM167 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM167 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2298] The complementary binding of VGAM167 RNA, herein designated VGAM RNA, to host target binding sites on VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM167 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2299] It is appreciated that VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM167 host target genes. The mRNA of each one of this plurality of VGAM167 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM167 RNA, herein designated VGAM RNA, and which when bound by VGAM167 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM167 host target proteins.

[2300] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM167 gene, herein designated VGAM GENE, on one or more VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2301] It is yet further appreciated that a function of VGAM167 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM167 correlate with, and may be deduced from, the identity of

the host target genes which VGAM167 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2302] Nucleotide sequences of the VGAM167 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM167 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM167 are further described hereinbelow with reference to Table 1.

[2303] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM167 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2304] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 168 (VGAM168) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2305] VGAM168 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM168 was detected is described hereinabove with reference to Figs. 2–8.

[2306] VGAM168 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2307] VGAM168 gene, herein designated VGAM GENE, encodes a VGAM168 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM168 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM168 precursor RNA is designated SEQ ID:3678, and is provided hereinbelow with reference to the sequence listing part.

[2308] VGAM168 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2309] An enzyme complex designated DICER COMPLEX, dices the VGAM168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM168 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM168 RNA is designated SEQ ID:3679, and is provided hereinbelow with reference to the sequence listing part.

[2310] VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2311] VGAM168 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM168 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2312] The complementary binding of VGAM168 RNA, herein designated VGAM RNA, to host target binding sites on VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM168 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2313] It is appreciated that VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM168 host target genes. The mRNA of each one of this plurality of VGAM168 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM168 RNA, herein designated VGAM RNA, and which when bound by VGAM168 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM168 host target proteins.

[2314] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM168 gene, herein designated VGAM GENE, on one or more VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2315] It is yet further appreciated that a function of VGAM168 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM168 correlate with, and may be deduced from, the identity of the host target genes which VGAM168 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[2316] Nucleotide sequences of the VGAM168 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM168 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM168 are further described hereinbelow with reference to Table 1.

[2317] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM168 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2318] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 169 (VGAM169) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2319] VGAM169 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM169 was detected is described hereinabove with reference to Figs. 2–8.

[2320] VGAM169 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM169 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2321] VGAM169 gene, herein designated VGAM GENE, encodes a VGAM169 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM169 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM169 precursor RNA is designated SEQ ID:3684, and is provided hereinbelow with reference to the sequence listing part.

[2322] VGAM169 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2323] An enzyme complex designated DICER COMPLEX, dices the VGAM169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM169 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM169 RNA is designated SEQ ID:3685, and is provided hereinbelow with reference to the sequence listing part.

[2324] VGAM169 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2325] VGAM169 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM169 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[2326] The complementary binding of VGAM169 RNA, herein designated VGAM RNA, to host target binding sites on VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM169 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2327] It is appreciated that VGAM169 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM169 host target genes. The mRNA of each one of this plurality of VGAM169 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM169 RNA, herein designated VGAM RNA, and which when bound by VGAM169 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM169 host target proteins.

[2328] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM169 gene, herein designated VGAM GENE, on one or more VGAM169 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2329] It is yet further appreciated that a function of VGAM169 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM169 correlate with, and may be deduced from, the identity of the host target genes which VGAM169 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[2330] Nucleotide sequences of the VGAM169 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM169 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM169 are further described hereinbelow with reference to Table 1.

[2331] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM169 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2332] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 170 (VGAM170) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2333] VGAM170 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The



method by which VGAM170 was detected is described hereinabove with reference to Figs. 2–8.

[2334] VGAM170 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM170 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2335] VGAM170 gene, herein designated VGAM GENE, encodes a VGAM170 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM170 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM170 precursor RNA is designated SEQ ID:3689, and is provided hereinbelow with reference to the sequence listing part.

[2336] VGAM170 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2337] An enzyme complex designated DICER COMPLEX, dices the VGAM170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM170 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM170 RNA is designated SEQ ID:3690, and is provided hereinbelow with reference to the sequence listing part.

[2338] VGAM170 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[2339] VGAM170 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM170 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM170 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2340] The complementary binding of VGAM170 RNA, herein designated VGAM RNA, to host target binding sites on VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM170 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2341] It is appreciated that VGAM170 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM170 host target genes. The mRNA of each one of this plurality of VGAM170 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM170 RNA, herein designated VGAM RNA, and which when bound by VGAM170 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM170 host target proteins.

[2342] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM170 gene, herein designated VGAM GENE, on one or

more VGAM170 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2343] It is yet further appreciated that a function of VGAM170 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM170 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM170 correlate with, and may be deduced from, the identity of the host target genes which VGAM170 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2344] Nucleotide sequences of the VGAM170 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM170 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM170 are further described hereinbelow with reference to Table 1.

[2345] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM170 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2346] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 171 (VGAM171) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2347] VGAM171 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM171 was detected is described

hereinabove with reference to Figs. 2–8.

[2348] VGAM171 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM171 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2349] VGAM171 gene, herein designated VGAM GENE, encodes a VGAM171 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM171 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM171 precursor RNA is designated SEQ ID:3709, and is provided hereinbelow with reference to the sequence listing part.

[2350] VGAM171 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2351] An enzyme complex designated DICER COMPLEX, dices the VGAM171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM171 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM171 RNA is designated SEQ ID:3710, and is provided hereinbelow with reference to the sequence listing part.

[2352] VGAM171 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.



[2353] VGAM171 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM171 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2354] The complementary binding of VGAM171 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM171 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2355] It is appreciated that VGAM171 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM171 host target genes. The mRNA of each one of this plurality of VGAM171 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM171 RNA, herein designated VGAM RNA, and which when bound by VGAM171 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM171 host target proteins.

[2356] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM171 gene, herein designated VGAM GENE, on one or more VGAM171 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2357] It is yet further appreciated that a function of VGAM171 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM171 correlate with, and may be deduced from, the identity of the host target genes which VGAM171 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2358] Nucleotide sequences of the VGAM171 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM171 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM171 are further described hereinbelow with reference to Table 1.

[2359] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM171 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2360] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 172 (VGAM172) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2361] VGAM172 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM172 was detected is described hereinabove with reference to Figs. 2-8.

[2362] VGAM172 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2363] VGAM172 gene, herein designated VGAM GENE, encodes a VGAM172 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM172 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM172 precursor RNA is designated SEQ ID:3714, and is provided hereinbelow with reference to the sequence listing part.

[2364] VGAM172 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[2365] An enzyme complex designated DICER COMPLEX, dices the VGAM172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM172 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM172 RNA is designated SEQ ID:3715, and is provided hereinbelow with reference to the sequence listing part.

[2366] VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2367] VGAM172 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM172 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2368] The complementary binding of VGAM172 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM172 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2369] It is appreciated that VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM172 host target genes. The mRNA of each one of this plurality of VGAM172 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM172 RNA, herein designated VGAM RNA, and which when bound by VGAM172 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM172 host target proteins.

[2370] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM172 gene, herein designated VGAM GENE, on one or more VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2371] It is yet further appreciated that a function of VGAM172 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM172 correlate with, and may be deduced from, the identity of the host target genes which VGAM172 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2372] Nucleotide sequences of the VGAM172 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM172 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM172 are further described hereinbelow with reference to Table 1.

[2373] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM172 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2374] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 173 (VGAM173) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2375] VGAM173 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM173 was detected is described hereinabove with reference to Figs. 2-8.

[2376] VGAM173 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Rana tigrina* ranavirus. VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2377] VGAM173 gene, herein designated VGAM GENE, encodes a VGAM173 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM173 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM173 precursor RNA is designated SEQ ID:3748, and is provided hereinbelow with reference to the sequence listing part.

[2378] VGAM173 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2379] An enzyme complex designated DICER COMPLEX, dices the VGAM173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM173 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM173 RNA is designated SEQ ID:3749, and is provided hereinbelow with reference to the sequence listing part.

[2380] VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2381] VGAM173 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM173 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2382] The complementary binding of VGAM173 RNA, herein designated VGAM RNA, to host target binding sites on VGAM173 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM173 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2383] It is appreciated that VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM173 host target genes. The mRNA of each one of this plurality of VGAM173 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM173 RNA, herein designated VGAM RNA, and which when bound by VGAM173 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM173 host target proteins.

[2384] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM173 gene, herein designated VGAM GENE, on one or more VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2385] It is yet further appreciated that a function of VGAM173 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM173 correlate with, and may be deduced from, the identity of the host target genes which VGAM173 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2386] Nucleotide sequences of the VGAM173 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM173 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM173 are further described hereinbelow with reference to Table 1.

[2387] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM173 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2388] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 174 (VGAM174) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2389] VGAM174 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM174 was detected is described hereinabove with reference to Figs. 2-8.

[2390] VGAM174 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus



1. VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2391] VGAM174 gene, herein designated VGAM GENE, encodes a VGAM174 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM174 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM174 precursor RNA is designated SEQ ID:3782, and is provided hereinbelow with reference to the sequence listing part.

[2392] VGAM174 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2393] An enzyme complex designated DICER COMPLEX, dices

the VGAM174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM174 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM174 RNA is designated SEQ ID:3783, and is provided hereinbelow with reference to the sequence listing part.

[2394] VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2395] VGAM174 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM174 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM174 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM174 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2396] The complementary binding of VGAM174 RNA, herein designated VGAM RNA, to host target binding sites on VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM174 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2397] It is appreciated that VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM174 host target genes. The mRNA of each one of this plurality of VGAM174 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM174 RNA, herein designated VGAM RNA, and which when bound by VGAM174 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM174 host target proteins.

[2398] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM174 gene, herein designated VGAM GENE, on one or more VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2399] It is yet further appreciated that a function of VGAM174 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM174 correlate with, and may be deduced from, the identity of the host target genes which VGAM174 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2400] Nucleotide sequences of the VGAM174 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM174 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM174 are further described hereinbelow with reference to Table 1.

[2401] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM174 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2402] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 175 (VGAM175) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2403] VGAM175 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM175 was detected is described hereinabove with reference to Figs. 2-8.

[2404] VGAM175 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM175 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[2405] VGAM175 gene, herein designated VGAM GENE, encodes a VGAM175 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM175 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM175 precursor RNA is designated SEQ ID:3808, and is provided hereinbelow with reference to the sequence listing part.

[2406] VGAM175 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2407] An enzyme complex designated DICER COMPLEX, dices the VGAM175 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM175 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM175 RNA is designated SEQ ID:3809, and is provided hereinbelow with reference to the sequence listing part.

[2408] VGAM175 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2409] VGAM175 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM175 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2410] The complementary binding of VGAM175 RNA, herein designated VGAM RNA, to host target binding sites on VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM175 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM175 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2411] It is appreciated that VGAM175 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM175 host target genes. The mRNA of each one of this plurality of VGAM175 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM175 RNA, herein designated VGAM RNA, and which when bound by VGAM175 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM175 host target proteins.

[2412] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM175 gene, herein designated VGAM GENE, on one or more VGAM175 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2413] It is yet further appreciated that a function of VGAM175 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM175 correlate with, and may be deduced from, the identity of the host target genes which VGAM175 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2414] Nucleotide sequences of the VGAM175 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM175 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM175 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM175 are further described hereinbelow with reference to Table 1.

[2415] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM175 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2416] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 176 (VGAM176) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2417] VGAM176 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM176 was detected is described hereinabove with reference to Figs. 2-8.

[2418] VGAM176 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM176 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[2419] VGAM176 gene, herein designated VGAM GENE, encodes a VGAM176 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM176 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM176 precursor RNA is designated SEQ ID:3878, and is provided hereinbelow with reference to the sequence listing part.

[2420] VGAM176 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2421] An enzyme complex designated DICER COMPLEX, dices the VGAM176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM176 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM176 RNA is designated SEQ ID:3879, and is provided hereinbelow with reference to the sequence listing part.

[2422] VGAM176 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM176 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM176 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2423] VGAM176 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM176 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM176 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM176 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM176 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2424] The complementary binding of VGAM176 RNA, herein designated VGAM RNA, to host target binding sites on VGAM176 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM176 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM176 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2425] It is appreciated that VGAM176 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM176 host target genes. The mRNA of each one of this plurality of VGAM176 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM176 RNA, herein designated VGAM RNA, and which when bound by VGAM176 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM176 host target proteins.

[2426] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM176 gene, herein designated VGAM GENE, on one or more VGAM176 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2427] It is yet further appreciated that a function of VGAM176 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM176 correlate with, and may be deduced from, the identity of the host target genes which VGAM176 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2428] Nucleotide sequences of the VGAM176 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM176 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM176 are further de-

scribed hereinbelow with reference to Table 1.

[2429] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM176 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2430] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 177 (VGAM177) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2431] VGAM177 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM177 was detected is described hereinabove with reference to Figs. 2-8.

[2432] VGAM177 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2433] VGAM177 gene, herein designated VGAM GENE, encodes a VGAM177 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM177 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM177 precursor RNA is designated SEQ ID:3886, and is provided hereinbelow with reference to the sequence listing part.

[2434] VGAM177 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2435] An enzyme complex designated DICER COMPLEX, dices the VGAM177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM177 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM177 RNA is designated SEQ ID:3887, and is provided hereinbelow with reference to the sequence listing part.

[2436] VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2437] VGAM177 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM177 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM177 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2438] The complementary binding of VGAM177 RNA, herein designated VGAM RNA, to host target binding sites on VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM177 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2439] It is appreciated that VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM177 host target genes. The mRNA of each one of this plurality of VGAM177 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM177 RNA, herein designated VGAM RNA, and which when bound by VGAM177 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM177 host target proteins.

[2440] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM177 gene, herein designated VGAM GENE, on one or more VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2441] It is yet further appreciated that a function of VGAM177 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM177 correlate with, and may be deduced from, the identity of the host target genes which VGAM177 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2442] Nucleotide sequences of the VGAM177 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM177 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM177 are further described hereinbelow with reference to Table 1.

[2443] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM177 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2444] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 178 (VGAM178) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2445] VGAM178 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM178 was detected is described hereinabove with reference to Figs. 2-8.

[2446] VGAM178 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2447] VGAM178 gene, herein designated VGAM GENE, encodes a



VGAM178 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM178 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM178 precursor RNA is designated SEQ ID:3934, and is provided hereinbelow with reference to the sequence listing part.

[2448] VGAM178 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2449] An enzyme complex designated DICER COMPLEX, dices the VGAM178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM178 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM178 RNA is designated SEQ ID:3935, and is provided hereinbelow with reference to the sequence listing part.

[2450] VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2451] VGAM178 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM178 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2452] The complementary binding of VGAM178 RNA, herein designated VGAM RNA, to host target binding sites on VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM178 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[2453] It is appreciated that VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM178 host target genes. The mRNA of each one of this plurality of VGAM178 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM178 RNA, herein designated VGAM RNA, and which when bound by VGAM178 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM178 host target proteins.

[2454] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM178 gene, herein designated VGAM GENE, on one or more VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2455] It is yet further appreciated that a function of VGAM178 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM178 correlate with, and may be deduced from, the identity of the host target genes which VGAM178 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2456] Nucleotide sequences of the VGAM178 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM178 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM178 are further described hereinbelow with reference to Table 1.

[2457] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM178 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2458] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 179 (VGAM179) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2459] VGAM179 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM179 was detected is described hereinabove with reference to Figs. 2-8.

[2460] VGAM179 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM179 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2461] VGAM179 gene, herein designated VGAM GENE, encodes a VGAM179 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM179 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM179 precursor RNA is designated SEQ ID:3953, and is provided hereinbelow with reference to the sequence listing part.

[2462] VGAM179 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2463] An enzyme complex designated DICER COMPLEX, dices the VGAM179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM179 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM179 RNA is designated SEQ ID:3954, and is provided hereinbelow with reference to the sequence listing part.

[2464] VGAM179 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2465] VGAM179 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host



target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM179 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2466] The complementary binding of VGAM179 RNA, herein designated VGAM RNA, to host target binding sites on VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM179 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2467] It is appreciated that VGAM179 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM179 host target genes. The mRNA of each one of this plurality of VGAM179 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM179 RNA, herein designated VGAM RNA, and which when bound by VGAM179 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM179 host target proteins.

[2468] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM179 gene, herein designated VGAM GENE, on one or more VGAM179 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2469] It is yet further appreciated that a function of VGAM179 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of viral infection by Molluscum contagiosum virus. Specific functions, and accordingly utilities, of VGAM179 correlate with, and may be deduced from, the identity of the host target genes which VGAM179 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2470] Nucleotide sequences of the VGAM179 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM179 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM179 are further described hereinbelow with reference to Table 1.

[2471] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM179 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2472] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 180 (VGAM180) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2473] VGAM180 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM180 was detected is described hereinabove with reference to Figs. 2–8.

[2474] VGAM180 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM180 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2475] VGAM180 gene, herein designated VGAM GENE, encodes a VGAM180 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM180 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM180 precursor RNA is designated SEQ ID:3966, and is provided hereinbelow with reference to the sequence listing part.

[2476] VGAM180 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2477] An enzyme complex designated DICER COMPLEX, dices the VGAM180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM180 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM180 RNA is designated SEQ ID:3967, and is provided hereinbelow with reference to the sequence listing part.

[2478] VGAM180 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2479] VGAM180 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM180 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2480] The complementary binding of VGAM180 RNA, herein designated VGAM RNA, to host target binding sites on VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM180 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2481] It is appreciated that VGAM180 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM180 host target genes. The mRNA of each one of this plurality of VGAM180 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM180 RNA, herein designated VGAM RNA, and which when bound by VGAM180 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM180 host target proteins.

[2482] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM180 gene, herein designated VGAM GENE, on one or more VGAM180 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2483] It is yet further appreciated that a function of VGAM180 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM180 correlate with, and may be deduced from, the identity of the host target genes which VGAM180 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2484] Nucleotide sequences of the VGAM180 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM180 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM180 are further described hereinbelow with reference to Table 1.

[2485] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM180 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2486] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 181 (VGAM181) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2487] VGAM181 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM181 was detected is described hereinabove with reference to Figs. 2–8.

[2488] VGAM181 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2489] VGAM181 gene, herein designated VGAM GENE, encodes a VGAM181 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM181 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM181 precursor RNA is designated SEQ ID:3997, and is provided hereinbelow with reference to the sequence listing part.

[2490] VGAM181 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2491] An enzyme complex designated DICER COMPLEX, dices the VGAM181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM181 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM181 RNA is designated SEQ ID:3998, and is provided hereinbelow with reference to the sequence listing part.

[2492] VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2493] VGAM181 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM181 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM181 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2494] The complementary binding of VGAM181 RNA, herein designated VGAM RNA, to host target binding sites on VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM181 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2495] It is appreciated that VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM181 host target genes. The mRNA of each one of this plurality of VGAM181 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM181 RNA, herein designated VGAM RNA, and which when bound by VGAM181 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM181 host target proteins.

[2496] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM181 gene, herein designated VGAM GENE, on one or more VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[2497] It is yet further appreciated that a function of VGAM181 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM181 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM181 correlate with, and may be deduced from, the identity of the host target genes which VGAM181 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2498] Nucleotide sequences of the VGAM181 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM181 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM181 are further described hereinbelow with reference to Table 1.

[2499] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM181 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2500] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 182 (VGAM182) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2501] VGAM182 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM182 was detected is described hereinabove with reference to Figs. 2–8.

[2502] VGAM182 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2503] VGAM182 gene, herein designated VGAM GENE, encodes a VGAM182 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM182 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a



protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM182 precursor RNA is designated SEQ ID:4027, and is provided hereinbelow with reference to the sequence listing part.

[2504] VGAM182 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2505] An enzyme complex designated DICER COMPLEX, dices the VGAM182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM182 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide se-

quence of VGAM182 RNA is designated SEQ ID:4028, and is provided hereinbelow with reference to the sequence listing part.

[2506] VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2507] VGAM182 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM182 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2508] The complementary binding of VGAM182 RNA, herein designated VGAM RNA, to host target binding sites on VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM182 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2509] It is appreciated that VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM182 host target genes. The mRNA of

each one of this plurality of VGAM182 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM182 RNA, herein designated VGAM RNA, and which when bound by VGAM182 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM182 host target proteins.

[2510] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM182 gene, herein designated VGAM GENE, on one or more VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[2511] It is yet further appreciated that a function of VGAM182 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM182 correlate with, and may be deduced from, the identity of the host target genes which VGAM182 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2512] Nucleotide sequences of the VGAM182 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM182 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM182 are further described hereinbelow with reference to Table 1.

[2513] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM182 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[2514] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 183 (VGAM183) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2515] VGAM183 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM183 was detected is described hereinabove with reference to Figs. 2–8.

[2516] VGAM183 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2517] VGAM183 gene, herein designated VGAM GENE, encodes a VGAM183 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM183 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM183 precursor RNA is designated SEQ ID:4042, and is provided hereinbelow with reference to the sequence listing part.

[2518] VGAM183 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2519] An enzyme complex designated DICER COMPLEX, dices the VGAM183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM183 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM183 RNA is designated SEQ ID:4043, and

is provided hereinbelow with reference to the sequence listing part.

[2520] VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2521] VGAM183 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM183 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM183 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2522] The complementary binding of VGAM183 RNA, herein designated VGAM RNA, to host target binding sites on VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM183 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2523] It is appreciated that VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM183 host target genes. The mRNA of each one of this plurality of VGAM183 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM183 RNA, herein designated VGAM RNA, and which when bound by VGAM183 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM183 host target proteins.

[2524] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM183 gene, herein designated VGAM GENE, on one or more VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2525] It is yet further appreciated that a function of VGAM183 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM183 correlate with, and may be deduced from, the identity of the host target genes which VGAM183 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2526] Nucleotide sequences of the VGAM183 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM183 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM183 are further described hereinbelow with reference to Table 1.

[2527] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM183 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2528] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 184 (VGAM184) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2529] VGAM184 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM184 was detected is described hereinabove with reference to Figs. 2–8.

[2530] VGAM184 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2531] VGAM184 gene, herein designated VGAM GENE, encodes a VGAM184 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM184 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM184 precursor RNA is

designated SEQ ID:4055, and is provided hereinbelow with reference to the sequence listing part.

[2532] VGAM184 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2533] An enzyme complex designated DICER COMPLEX, dices the VGAM184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM184 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM184 RNA is designated SEQ ID:4056, and is provided hereinbelow with reference to the sequence

listing part.

[2534] VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2535] VGAM184 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM184 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2536] The complementary binding of VGAM184 RNA, herein designated VGAM RNA, to host target binding sites on VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM184 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2537] It is appreciated that VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM184 host target genes. The mRNA of each one of this plurality of VGAM184 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM184 RNA, herein designated VGAM RNA, and which when bound by VGAM184 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM184 host target proteins.

[2538] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM184 gene, herein designated VGAM GENE, on one or more VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2539] It is yet further appreciated that a function of VGAM184 is



inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM184 correlate with, and may be deduced from, the identity of the host target genes which VGAM184 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2540] Nucleotide sequences of the VGAM184 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM184 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM184 are further described hereinbelow with reference to Table 1.

[2541] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM184 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2542] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 185 (VGAM185) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2543] VGAM185 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM185 was detected is described hereinabove with reference to Figs. 2–8.

[2544] VGAM185 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2545] VGAM185 gene, herein designated VGAM GENE, encodes a VGAM185 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM185 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM185 precursor RNA is designated SEQ ID:4072, and is provided hereinbelow with

reference to the sequence listing part.

[2546] VGAM185 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2547] An enzyme complex designated DICER COMPLEX, dices the VGAM185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM185 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM185 RNA is designated SEQ ID:4073, and is provided hereinbelow with reference to the sequence listing part.

[2548] VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2549] VGAM185 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM185 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM185 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2550] The complementary binding of VGAM185 RNA, herein designated VGAM RNA, to host target binding sites on VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM185 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2551] It is appreciated that VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM185 host target genes. The mRNA of each one of this plurality of VGAM185 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM185 RNA, herein designated VGAM RNA, and which when bound by VGAM185 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM185 host target proteins.

[2552] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM185 gene, herein designated VGAM GENE, on one or more VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2553] It is yet further appreciated that a function of VGAM185 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM185 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM185 correlate with, and may be deduced from, the identity of the host target genes which VGAM185 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2554] Nucleotide sequences of the VGAM185 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM185 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM185 are further described hereinbelow with reference to Table 1.

[2555] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM185 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2556] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 186 (VGAM186) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2557] VGAM186 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM186 was detected is described hereinabove with reference to Figs. 2–8.

[2558] VGAM186 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM186 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2559] VGAM186 gene, herein designated VGAM GENE, encodes a VGAM186 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM186 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM186 precursor RNA is designated SEQ ID:4075, and is provided hereinbelow with reference to the sequence listing part.



[2560] VGAM186 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2561] An enzyme complex designated DICER COMPLEX, dices the VGAM186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM186 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM186 RNA is designated SEQ ID:4076, and is provided hereinbelow with reference to the sequence listing part.

[2562] VGAM186 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM186 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM186 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2563] VGAM186 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM186 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM186 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM186 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2564] The complementary binding of VGAM186 RNA, herein designated VGAM RNA, to host target binding sites on VGAM186 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM186 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM186 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2565] It is appreciated that VGAM186 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM186 host target genes. The mRNA of each one of this plurality of VGAM186 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM186 RNA, herein designated VGAM

RNA, and which when bound by VGAM186 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM186 host target proteins.

[2566] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM186 gene, herein designated VGAM GENE, on one or more VGAM186 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2567] It is yet further appreciated that a function of VGAM186 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM186 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM186 correlate with, and may be deduced from, the identity of the host target genes which VGAM186 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2568] Nucleotide sequences of the VGAM186 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM186 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM186 are further described hereinbelow with reference to Table 1.

[2569] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM186 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2570] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 187 (VGAM187) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2571] VGAM187 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM187 was detected is described hereinabove with reference to Figs. 2–8.

[2572] VGAM187 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2573] VGAM187 gene, herein designated VGAM GENE, encodes a VGAM187 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM187 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM187 precursor RNA is designated SEQ ID:4097, and is provided hereinbelow with reference to the sequence listing part.

[2574] VGAM187 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2575] An enzyme complex designated DICER COMPLEX, dices the VGAM187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM187 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM187 RNA is designated SEQ ID:4098, and is provided hereinbelow with reference to the sequence listing part.

[2576] VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2577] VGAM187 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM187 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM187 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM187 host



target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2578] The complementary binding of VGAM187 RNA, herein designated VGAM RNA, to host target binding sites on VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM187 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2579] It is appreciated that VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM187 host target genes. The mRNA of each one of this plurality of VGAM187 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM187 RNA, herein designated VGAM RNA, and which when bound by VGAM187 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM187 host target proteins.

[2580] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM187 gene, herein designated VGAM GENE, on one or more VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2581] It is yet further appreciated that a function of VGAM187 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM187 include diagnosis, prevention and

treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM187 correlate with, and may be deduced from, the identity of the host target genes which VGAM187 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2582] Nucleotide sequences of the VGAM187 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM187 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM187 are further described hereinbelow with reference to Table 1.

[2583] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM187 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2584] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 188 (VGAM188) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2585] VGAM188 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM188 was detected is described hereinabove with reference to Figs. 2–8.

[2586] VGAM188 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2587] VGAM188 gene, herein designated VGAM GENE, encodes a VGAM188 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM188 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM188 precursor RNA is designated SEQ ID:4105, and is provided hereinbelow with reference to the sequence listing part.

[2588] VGAM188 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM188 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2589] An enzyme complex designated DICER COMPLEX, dices the VGAM188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM188 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM188 RNA is designated SEQ ID:4106, and is provided hereinbelow with reference to the sequence listing part.

[2590] VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM188 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2591] VGAM188 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM188 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM188 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2592] The complementary binding of VGAM188 RNA, herein designated VGAM RNA, to host target binding sites on VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM188 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2593] It is appreciated that VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM188 host target genes. The mRNA of each one of this plurality of VGAM188 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM188 RNA, herein designated VGAM RNA, and which when bound by VGAM188 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM188 host target proteins.

[2594] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM188 gene, herein designated VGAM GENE, on one or more VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2595] It is yet further appreciated that a function of VGAM188 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM188 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1.



Specific functions, and accordingly utilities, of VGAM188 correlate with, and may be deduced from, the identity of the host target genes which VGAM188 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2596] Nucleotide sequences of the VGAM188 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM188 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM188 are further described hereinbelow with reference to Table 1.

[2597] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM188 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2598] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 189 (VGAM189) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[2599] VGAM189 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM189 was detected is described hereinabove with reference to Figs. 2–8.

[2600] VGAM189 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2601] VGAM189 gene, herein designated VGAM GENE, encodes a VGAM189 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM189 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM189 precursor RNA is designated SEQ ID:4220, and is provided hereinbelow with reference to the sequence listing part.

[2602] VGAM189 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM189 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2603] An enzyme complex designated DICER COMPLEX, dices the VGAM189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM189 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM189 RNA is designated SEQ ID:4221, and is provided hereinbelow with reference to the sequence listing part.

[2604] VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM189 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2605] VGAM189 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM189 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2606] The complementary binding of VGAM189 RNA, herein designated VGAM RNA, to host target binding sites on VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM189 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2607] It is appreciated that VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM189 host target genes. The mRNA of each one of this plurality of VGAM189 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM189 RNA, herein designated VGAM RNA, and which when bound by VGAM189 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM189 host target proteins.

[2608] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM189 gene, herein designated VGAM GENE, on one or more VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2609] It is yet further appreciated that a function of VGAM189 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM189

correlate with, and may be deduced from, the identity of the host target genes which VGAM189 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2610] Nucleotide sequences of the VGAM189 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM189 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM189 are further described hereinbelow with reference to Table 1.

[2611] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM189 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2612] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 190 (VGAM190) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[2613] VGAM190 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM190 was detected is described hereinabove with reference to Figs. 2–8.

[2614] VGAM190 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2615] VGAM190 gene, herein designated VGAM GENE, encodes a VGAM190 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM190 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM190 precursor RNA is designated SEQ ID:4227, and is provided hereinbelow with reference to the sequence listing part.

[2616] VGAM190 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.



As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2617] An enzyme complex designated DICER COMPLEX, dices the VGAM190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM190 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM190 RNA is designated SEQ ID:4228, and is provided hereinbelow with reference to the sequence listing part.

[2618] VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2619] VGAM190 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM190 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2620] The complementary binding of VGAM190 RNA, herein designated VGAM RNA, to host target binding sites on VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM190 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2621] It is appreciated that VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM190 host target genes. The mRNA of each one of this plurality of VGAM190 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM190 RNA, herein designated VGAM RNA, and which when bound by VGAM190 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM190 host target proteins.

[2622] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM190 gene, herein designated VGAM GENE, on one or more VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2623] It is yet further appreciated that a function of VGAM190 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM190 correlate with, and may be deduced from, the identity of

the host target genes which VGAM190 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2624] Nucleotide sequences of the VGAM190 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM190 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM190 are further described hereinbelow with reference to Table 1.

[2625] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM190 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2626] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 191 (VGAM191) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2627] VGAM191 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM191 was detected is described hereinabove with reference to Figs. 2–8.

[2628] VGAM191 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM191 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2629] VGAM191 gene, herein designated VGAM GENE, encodes a VGAM191 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM191 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM191 precursor RNA is designated SEQ ID:4247, and is provided hereinbelow with reference to the sequence listing part.

[2630] VGAM191 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2631] An enzyme complex designated DICER COMPLEX, dices the VGAM191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM191 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM191 RNA is designated SEQ ID:4248, and is provided hereinbelow with reference to the sequence listing part.

[2632] VGAM191 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2633] VGAM191 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM191 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-



cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2634] The complementary binding of VGAM191 RNA, herein designated VGAM RNA, to host target binding sites on VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM191 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2635] It is appreciated that VGAM191 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM191 host target genes. The mRNA of each one of this plurality of VGAM191 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM191 RNA, herein designated VGAM RNA, and which when bound by VGAM191 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM191 host target proteins.

[2636] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM191 gene, herein designated VGAM GENE, on one or more VGAM191 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2637] It is yet further appreciated that a function of VGAM191 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM191 correlate with, and may be deduced from, the identity of the host target genes which VGAM191 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[2638] Nucleotide sequences of the VGAM191 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM191 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM191 are further described hereinbelow with reference to Table 1.

[2639] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM191 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2640] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 192 (VGAM192) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2641] VGAM192 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM192 was detected is described hereinabove with reference to Figs. 2–8.

[2642] VGAM192 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2643] VGAM192 gene, herein designated VGAM GENE, encodes a VGAM192 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM192 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM192 precursor RNA is designated SEQ ID:4253, and is provided hereinbelow with reference to the sequence listing part.

[2644] VGAM192 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2645] An enzyme complex designated DICER COMPLEX, dices the VGAM192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM192 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM192 RNA is designated SEQ ID:4254, and is provided hereinbelow with reference to the sequence listing part.

[2646] VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2647] VGAM192 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM192 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM192 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[2648] The complementary binding of VGAM192 RNA, herein designated VGAM RNA, to host target binding sites on VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM192 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2649] It is appreciated that VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM192 host target genes. The mRNA of each one of this plurality of VGAM192 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM192 RNA, herein designated VGAM RNA, and which when bound by VGAM192 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM192 host target proteins.

[2650] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM192 gene, herein designated VGAM GENE, on one or more VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2651] It is yet further appreciated that a function of VGAM192 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM192 correlate with, and may be deduced from, the identity of the host target genes which VGAM192 binds and inhibits, and the function of these host target genes, as elaborated



hereinbelow.

[2652] Nucleotide sequences of the VGAM192 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM192 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM192 are further described hereinbelow with reference to Table 1.

[2653] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM192 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2654] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 193 (VGAM193) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2655] VGAM193 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM193 was detected is described hereinabove with reference to Figs. 2–8.

[2656] VGAM193 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 1. VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2657] VGAM193 gene, herein designated VGAM GENE, encodes a VGAM193 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM193 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM193 precursor RNA is designated SEQ ID:4263, and is provided hereinbelow with reference to the sequence listing part.

[2658] VGAM193 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2659] An enzyme complex designated DICER COMPLEX, dices the VGAM193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM193 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM193 RNA is designated SEQ ID:4264, and is provided hereinbelow with reference to the sequence listing part.

[2660] VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[2661] VGAM193 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM193 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2662] The complementary binding of VGAM193 RNA, herein designated VGAM RNA, to host target binding sites on VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM193 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2663] It is appreciated that VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM193 host target genes. The mRNA of each one of this plurality of VGAM193 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM193 RNA, herein designated VGAM RNA, and which when bound by VGAM193 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM193 host target proteins.

[2664] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM193 gene, herein designated VGAM GENE, on one or

more VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2665] It is yet further appreciated that a function of VGAM193 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 1. Specific functions, and accordingly utilities, of VGAM193 correlate with, and may be deduced from, the identity of the host target genes which VGAM193 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2666] Nucleotide sequences of the VGAM193 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM193 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM193 are further described hereinbelow with reference to Table 1.

[2667] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM193 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2668] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 194 (VGAM194) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2669] VGAM194 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM194 was detected is described

hereinabove with reference to Figs. 2–8.

[2670] VGAM194 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox virus.

VGAM194 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2671] VGAM194 gene, herein designated VGAM GENE, encodes a VGAM194 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM194 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM194 precursor RNA is designated SEQ ID:4448, and is provided hereinbelow with reference to the sequence listing part.

[2672] VGAM194 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed–reversed sequence of the nucleotide sequence of the second half thereof.

[2673] An enzyme complex designated DICER COMPLEX, dices the VGAM194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM194 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM194 RNA is designated SEQ ID:4449, and is provided hereinbelow with reference to the sequence listing part.

[2674] VGAM194 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2675] VGAM194 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM194 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2676] The complementary binding of VGAM194 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM194 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2677] It is appreciated that VGAM194 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM194 host target genes. The mRNA of each one of this plurality of VGAM194 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM194 RNA, herein designated VGAM RNA, and which when bound by VGAM194 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM194 host target proteins.

[2678] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM194 gene, herein designated VGAM GENE, on one or more VGAM194 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2679] It is yet further appreciated that a function of VGAM194 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific functions, and accordingly utilities, of VGAM194 correlate with, and may be deduced from, the identity of the host target genes which VGAM194 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2680] Nucleotide sequences of the VGAM194 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM194 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM194 are further described hereinbelow with reference to Table 1.

[2681] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM194 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2682] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 195 (VGAM195) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2683] VGAM195 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM195 was detected is described hereinabove with reference to Figs. 2-8.

[2684] VGAM195 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM195 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2685] VGAM195 gene, herein designated VGAM GENE, encodes a VGAM195 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM195 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM195 precursor RNA is designated SEQ ID:4454, and is provided hereinbelow with reference to the sequence listing part.

[2686] VGAM195 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[2687] An enzyme complex designated DICER COMPLEX, dices the VGAM195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM195 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM195 RNA is designated SEQ ID:4455, and is provided hereinbelow with reference to the sequence listing part.

[2688] VGAM195 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2689] VGAM195 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM195 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM195 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2690] The complementary binding of VGAM195 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM195 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2691] It is appreciated that VGAM195 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM195 host target genes. The mRNA of each one of this plurality of VGAM195 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM195 RNA, herein designated VGAM RNA, and which when bound by VGAM195 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM195 host target proteins.

[2692] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM195 gene, herein designated VGAM GENE, on one or more VGAM195 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2693] It is yet further appreciated that a function of VGAM195 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM195 correlate with, and may be deduced from, the identity of the host target genes which VGAM195 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2694] Nucleotide sequences of the VGAM195 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM195 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM195 are further described hereinbelow with reference to Table 1.

[2695] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM195 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2696] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 196 (VGAM196) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2697] VGAM196 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM196 was detected is described hereinabove with reference to Figs. 2-8.

[2698] VGAM196 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Bovine herpesvirus 1. VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2699] VGAM196 gene, herein designated VGAM GENE, encodes a VGAM196 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM196 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM196 precursor RNA is designated SEQ ID:4458, and is provided hereinbelow with reference to the sequence listing part.

[2700] VGAM196 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2701] An enzyme complex designated DICER COMPLEX, dices the VGAM196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM196 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM196 RNA is designated SEQ ID:4459, and is provided hereinbelow with reference to the sequence listing part.

[2702] VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2703] VGAM196 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM196 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2704] The complementary binding of VGAM196 RNA, herein designated VGAM RNA, to host target binding sites on VGAM196 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM196 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2705] It is appreciated that VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM196 host target genes. The mRNA of each one of this plurality of VGAM196 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM196 RNA, herein designated VGAM RNA, and which when bound by VGAM196 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM196 host target proteins.

[2706] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM196 gene, herein designated VGAM GENE, on one or more VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2707] It is yet further appreciated that a function of VGAM196 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM196 correlate with, and may be deduced from, the identity of the host target genes which VGAM196 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2708] Nucleotide sequences of the VGAM196 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM196 RNA, herein designated VGAM RNA, and a



schematic representation of the secondary folding of VGAM196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM196 are further described hereinbelow with reference to Table 1.

[2709] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM196 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2710] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 197 (VGAM197) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2711] VGAM197 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM197 was detected is described hereinabove with reference to Figs. 2-8.

[2712] VGAM197 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1.

VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2713] VGAM197 gene, herein designated VGAM GENE, encodes a VGAM197 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM197 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM197 precursor RNA is designated SEQ ID:4521, and is provided hereinbelow with reference to the sequence listing part.

[2714] VGAM197 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2715] An enzyme complex designated DICER COMPLEX, dices

the VGAM197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM197 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM197 RNA is designated SEQ ID:4522, and is provided hereinbelow with reference to the sequence listing part.

[2716] VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2717] VGAM197 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM197 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM197 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2718] The complementary binding of VGAM197 RNA, herein designated VGAM RNA, to host target binding sites on VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM197 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2719] It is appreciated that VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM197 host target genes. The mRNA of each one of this plurality of VGAM197 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM197 RNA, herein designated VGAM RNA, and which when bound by VGAM197 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM197 host target proteins.

[2720] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM197 gene, herein designated VGAM GENE, on one or more VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2721] It is yet further appreciated that a function of VGAM197 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM197 correlate with, and may be deduced from, the identity of the host target genes which VGAM197 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2722] Nucleotide sequences of the VGAM197 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM197 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM197 are further described hereinbelow with reference to Table 1.

[2723] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM197 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2724] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 198 (VGAM198) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2725] VGAM198 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM198 was detected is described hereinabove with reference to Figs. 2-8.

[2726] VGAM198 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM198 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[2727] VGAM198 gene, herein designated VGAM GENE, encodes a VGAM198 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM198 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM198 precursor RNA is designated SEQ ID:4538, and is provided hereinbelow with reference to the sequence listing part.

[2728] VGAM198 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2729] An enzyme complex designated DICER COMPLEX, dices the VGAM198 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM198 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM198 RNA is designated SEQ ID:4539, and is provided hereinbelow with reference to the sequence listing part.

[2730] VGAM198 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2731] VGAM198 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM198 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM198 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2732] The complementary binding of VGAM198 RNA, herein designated VGAM RNA, to host target binding sites on VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM198 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM198 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2733] It is appreciated that VGAM198 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM198 host target genes. The mRNA of each one of this plurality of VGAM198 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM198 RNA, herein designated VGAM RNA, and which when bound by VGAM198 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM198 host target proteins.

[2734] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM198 gene, herein designated VGAM GENE, on one or more VGAM198 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2735] It is yet further appreciated that a function of VGAM198 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM198 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM198 correlate with, and may be deduced from, the identity of the host target genes which VGAM198 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2736] Nucleotide sequences of the VGAM198 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM198 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM198 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM198 are further described hereinbelow with reference to Table 1.

[2737] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM198 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2738] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 199 (VGAM199) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2739] VGAM199 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM199 was detected is described hereinabove with reference to Figs. 2-8.

[2740] VGAM199 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM199 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[2741] VGAM199 gene, herein designated VGAM GENE, encodes a VGAM199 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM199 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM199 precursor RNA is designated SEQ ID:4577, and is provided hereinbelow with reference to the sequence listing part.

[2742] VGAM199 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2743] An enzyme complex designated DICER COMPLEX, dices the VGAM199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM199 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM199 RNA is designated SEQ ID:4578, and is provided hereinbelow with reference to the sequence listing part.

[2744] VGAM199 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2745] VGAM199 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM199 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM199 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2746] The complementary binding of VGAM199 RNA, herein designated VGAM RNA, to host target binding sites on VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA,



into VGAM199 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2747] It is appreciated that VGAM199 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM199 host target genes. The mRNA of each one of this plurality of VGAM199 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM199 RNA, herein designated VGAM RNA, and which when bound by VGAM199 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM199 host target proteins.

[2748] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM199 gene, herein designated VGAM GENE, on one or more VGAM199 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2749] It is yet further appreciated that a function of VGAM199 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM199 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM199 correlate with, and may be deduced from, the identity of the host target genes which VGAM199 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2750] Nucleotide sequences of the VGAM199 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM199 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM199 are further de-

scribed hereinbelow with reference to Table 1.

[2751] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM199 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2752] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 200 (VGAM200) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2753] VGAM200 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM200 was detected is described hereinabove with reference to Figs. 2-8.

[2754] VGAM200 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2755] VGAM200 gene, herein designated VGAM GENE, encodes a VGAM200 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM200 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM200 precursor RNA is designated SEQ ID:4582, and is provided hereinbelow with reference to the sequence listing part.

[2756] VGAM200 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2757] An enzyme complex designated DICER COMPLEX, dices the VGAM200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM200 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM200 RNA is designated SEQ ID:4583, and is provided hereinbelow with reference to the sequence listing part.

[2758] VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2759] VGAM200 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM200 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM200 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2760] The complementary binding of VGAM200 RNA, herein designated VGAM RNA, to host target binding sites on VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM200 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2761] It is appreciated that VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM200 host target genes. The mRNA of each one of this plurality of VGAM200 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM200 RNA, herein designated VGAM RNA, and which when bound by VGAM200 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM200 host target proteins.

[2762] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM200 gene, herein designated VGAM GENE, on one or more VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2763] It is yet further appreciated that a function of VGAM200 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM200 correlate with, and may be deduced from, the identity of the host target genes which VGAM200 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2764] Nucleotide sequences of the VGAM200 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM200 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM200 are further described hereinbelow with reference to Table 1.



[2765] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM200 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2766] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 201 (VGAM201) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2767] VGAM201 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM201 was detected is described hereinabove with reference to Figs. 2-8.

[2768] VGAM201 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2769] VGAM201 gene, herein designated VGAM GENE, encodes a

VGAM201 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM201 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM201 precursor RNA is designated SEQ ID:4634, and is provided hereinbelow with reference to the sequence listing part.

[2770] VGAM201 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2771] An enzyme complex designated DICER COMPLEX, dices the VGAM201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM201 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM201 RNA is designated SEQ ID:4635, and is provided hereinbelow with reference to the sequence listing part.

[2772] VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2773] VGAM201 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM201 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM201 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2774] The complementary binding of VGAM201 RNA, herein designated VGAM RNA, to host target binding sites on VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM201 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[2775] It is appreciated that VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM201 host target genes. The mRNA of each one of this plurality of VGAM201 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM201 RNA, herein designated VGAM RNA, and which when bound by VGAM201 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM201 host target proteins.

[2776] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM201 gene, herein designated VGAM GENE, on one or more VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2777] It is yet further appreciated that a function of VGAM201 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM201 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM201 correlate with, and may be deduced from, the identity of the host target genes which VGAM201 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2778] Nucleotide sequences of the VGAM201 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM201 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM201 are further described hereinbelow with reference to Table 1.

[2779] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM201 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2780] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 202 (VGAM202) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2781] VGAM202 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM202 was detected is described hereinabove with reference to Figs. 2-8.

[2782] VGAM202 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM202 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2783] VGAM202 gene, herein designated VGAM GENE, encodes a VGAM202 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM202 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM202 precursor RNA is designated SEQ ID:4652, and is provided hereinbelow with reference to the sequence listing part.

[2784] VGAM202 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2785] An enzyme complex designated DICER COMPLEX, dices the VGAM202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM202 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM202 RNA is designated SEQ ID:4653, and is provided hereinbelow with reference to the sequence listing part.

[2786] VGAM202 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2787] VGAM202 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM202 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM202 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2788] The complementary binding of VGAM202 RNA, herein designated VGAM RNA, to host target binding sites on VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM202 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2789] It is appreciated that VGAM202 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM202 host target genes. The mRNA of each one of this plurality of VGAM202 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM202 RNA, herein designated VGAM RNA, and which when bound by VGAM202 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM202 host target proteins.

[2790] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM202 gene, herein designated VGAM GENE, on one or more VGAM202 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2791] It is yet further appreciated that a function of VGAM202 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM202 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM202 correlate with, and may be deduced from, the identity of the host target genes which VGAM202 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2792] Nucleotide sequences of the VGAM202 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM202 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM202 are further described hereinbelow with reference to Table 1.

[2793] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM202 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2794] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 203 (VGAM203) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2795] VGAM203 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM203 was detected is described hereinabove with reference to Figs. 2–8.

[2796] VGAM203 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM203 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2797] VGAM203 gene, herein designated VGAM GENE, encodes a VGAM203 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM203 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM203 precursor RNA is designated SEQ ID:4683, and is provided hereinbelow with reference to the sequence listing part.

[2798] VGAM203 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2799] An enzyme complex designated DICER COMPLEX, dices the VGAM203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM203 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM203 RNA is designated SEQ ID:4684, and is provided hereinbelow with reference to the sequence listing part.

[2800] VGAM203 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2801] VGAM203 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM203 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM203 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2802] The complementary binding of VGAM203 RNA, herein designated VGAM RNA, to host target binding sites on VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM203 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2803] It is appreciated that VGAM203 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM203 host target genes. The mRNA of each one of this plurality of VGAM203 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM203 RNA, herein designated VGAM RNA, and which when bound by VGAM203 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM203 host target proteins.

[2804] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM203 gene, herein designated VGAM GENE, on one or more VGAM203 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2805] It is yet further appreciated that a function of VGAM203 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM203 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM203 correlate with, and may be deduced from, the identity of the host target genes which VGAM203 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2806] Nucleotide sequences of the VGAM203 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM203 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM203 are further described hereinbelow with reference to Table 1.

[2807] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM203 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2808] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 204 (VGAM204) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2809] VGAM204 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM204 was detected is described hereinabove with reference to Figs. 2–8.

[2810] VGAM204 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2811] VGAM204 gene, herein designated VGAM GENE, encodes a VGAM204 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM204 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM204 precursor RNA is designated SEQ ID:4731, and is provided hereinbelow with reference to the sequence listing part.

[2812] VGAM204 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2813] An enzyme complex designated DICER COMPLEX, dices the VGAM204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM204 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM204 RNA is designated SEQ ID:4732, and is provided hereinbelow with reference to the sequence listing part.

[2814] VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2815] VGAM204 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM204 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM204 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2816] The complementary binding of VGAM204 RNA, herein designated VGAM RNA, to host target binding sites on VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM204 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2817] It is appreciated that VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM204 host target genes. The mRNA of each one of this plurality of VGAM204 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM204 RNA, herein designated VGAM RNA, and which when bound by VGAM204 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM204 host target proteins.

[2818] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM204 gene, herein designated VGAM GENE, on one or more VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[2819] It is yet further appreciated that a function of VGAM204 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM204 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM204 correlate with, and may be deduced from, the identity of the host target genes which VGAM204 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2820] Nucleotide sequences of the VGAM204 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM204 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM204 are further described hereinbelow with reference to Table 1.

[2821] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM204 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2822] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 205 (VGAM205) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2823] VGAM205 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM205 was detected is described hereinabove with reference to Figs. 2–8.

[2824] VGAM205 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2825] VGAM205 gene, herein designated VGAM GENE, encodes a VGAM205 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM205 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM205 precursor RNA is designated SEQ ID:4765, and is provided hereinbelow with reference to the sequence listing part.

[2826] VGAM205 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2827] An enzyme complex designated DICER COMPLEX, dices the VGAM205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM205 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM205 RNA is designated SEQ ID:4766, and is provided hereinbelow with reference to the sequence listing part.

[2828] VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2829] VGAM205 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM205 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM205 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2830] The complementary binding of VGAM205 RNA, herein designated VGAM RNA, to host target binding sites on VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM205 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2831] It is appreciated that VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM205 host target genes. The mRNA of

each one of this plurality of VGAM205 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM205 RNA, herein designated VGAM RNA, and which when bound by VGAM205 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM205 host target proteins.

[2832] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM205 gene, herein designated VGAM GENE, on one or more VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[2833] It is yet further appreciated that a function of VGAM205 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM205 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM205 correlate with, and may be deduced from, the identity of the host target genes which VGAM205 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2834] Nucleotide sequences of the VGAM205 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM205 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM205 are further described hereinbelow with reference to Table 1.

[2835] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM205 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[2836] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 206 (VGAM206) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2837] VGAM206 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM206 was detected is described hereinabove with reference to Figs. 2–8.

[2838] VGAM206 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2839] VGAM206 gene, herein designated VGAM GENE, encodes a VGAM206 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM206 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM206 precursor RNA is designated SEQ ID:4775, and is provided hereinbelow with reference to the sequence listing part.

[2840] VGAM206 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2841] An enzyme complex designated DICER COMPLEX, dices the VGAM206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM206 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM206 RNA is designated SEQ ID:4776, and



is provided hereinbelow with reference to the sequence listing part.

[2842] VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2843] VGAM206 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM206 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2844] The complementary binding of VGAM206 RNA, herein designated VGAM RNA, to host target binding sites on VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM206 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2845] It is appreciated that VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM206 host target genes. The mRNA of each one of this plurality of VGAM206 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM206 RNA, herein designated VGAM RNA, and which when bound by VGAM206 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM206 host target proteins.

[2846] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM206 gene, herein designated VGAM GENE, on one or more VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2847] It is yet further appreciated that a function of VGAM206 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM206 correlate with, and may be deduced from, the identity of the host target genes which VGAM206 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2848] Nucleotide sequences of the VGAM206 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM206 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM206 are further described hereinbelow with reference to Table 1.

[2849] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM206 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2850] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 207 (VGAM207) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2851] VGAM207 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM207 was detected is described hereinabove with reference to Figs. 2–8.

[2852] VGAM207 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2853] VGAM207 gene, herein designated VGAM GENE, encodes a VGAM207 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM207 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM207 precursor RNA is

designated SEQ ID:4811, and is provided hereinbelow with reference to the sequence listing part.

[2854] VGAM207 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2855] An enzyme complex designated DICER COMPLEX, dices the VGAM207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM207 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM207 RNA is designated SEQ ID:4812, and is provided hereinbelow with reference to the sequence

listing part.

[2856] VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2857] VGAM207 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM207 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM207 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2858] The complementary binding of VGAM207 RNA, herein designated VGAM RNA, to host target binding sites on VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM207 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2859] It is appreciated that VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM207 host target genes. The mRNA of each one of this plurality of VGAM207 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM207 RNA, herein designated VGAM RNA, and which when bound by VGAM207 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM207 host target proteins.

[2860] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM207 gene, herein designated VGAM GENE, on one or more VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2861] It is yet further appreciated that a function of VGAM207 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM207 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM207 correlate with, and may be deduced from, the identity of the host target genes which VGAM207 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2862] Nucleotide sequences of the VGAM207 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM207 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM207 are further described hereinbelow with reference to Table 1.

[2863] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM207 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2864] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 208 (VGAM208) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2865] VGAM208 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM208 was detected is described hereinabove with reference to Figs. 2–8.

[2866] VGAM208 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2867] VGAM208 gene, herein designated VGAM GENE, encodes a VGAM208 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM208 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM208 precursor RNA is designated SEQ ID:4862, and is provided hereinbelow with

reference to the sequence listing part.

[2868] VGAM208 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2869] An enzyme complex designated DICER COMPLEX, dices the VGAM208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM208 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM208 RNA is designated SEQ ID:4863, and is provided hereinbelow with reference to the sequence listing part.

[2870] VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2871] VGAM208 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM208 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2872] The complementary binding of VGAM208 RNA, herein designated VGAM RNA, to host target binding sites on VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM208 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2873] It is appreciated that VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM208 host target genes. The mRNA of each one of this plurality of VGAM208 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM208 RNA, herein designated VGAM RNA, and which when bound by VGAM208 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM208 host target proteins.

[2874] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM208 gene, herein designated VGAM GENE, on one or more VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2875] It is yet further appreciated that a function of VGAM208 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM208 correlate with, and may be deduced from, the identity of the host target genes which VGAM208 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2876] Nucleotide sequences of the VGAM208 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM208 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM208 are further described hereinbelow with reference to Table 1.

[2877] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM208 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2878] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 209 (VGAM209) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2879] VGAM209 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM209 was detected is described hereinabove with reference to Figs. 2–8.

[2880] VGAM209 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM209 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2881] VGAM209 gene, herein designated VGAM GENE, encodes a VGAM209 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM209 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM209 precursor RNA is designated SEQ ID:4869, and is provided hereinbelow with reference to the sequence listing part.

[2882] VGAM209 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2883] An enzyme complex designated DICER COMPLEX, dices the VGAM209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM209 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM209 RNA is designated SEQ ID:4870, and is provided hereinbelow with reference to the sequence listing part.

[2884] VGAM209 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2885] VGAM209 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM209 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM209 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2886] The complementary binding of VGAM209 RNA, herein designated VGAM RNA, to host target binding sites on VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM209 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2887] It is appreciated that VGAM209 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM209 host target genes. The mRNA of each one of this plurality of VGAM209 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM209 RNA, herein designated VGAM

RNA, and which when bound by VGAM209 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM209 host target proteins.

[2888] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM209 gene, herein designated VGAM GENE, on one or more VGAM209 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2889] It is yet further appreciated that a function of VGAM209 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM209 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM209 correlate with, and may be deduced from, the identity of the host target genes which VGAM209 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2890] Nucleotide sequences of the VGAM209 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM209 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM209 are further described hereinbelow with reference to Table 1.

[2891] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM209 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2892] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 210 (VGAM210) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2893] VGAM210 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM210 was detected is described hereinabove with reference to Figs. 2–8.

[2894] VGAM210 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM210 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2895] VGAM210 gene, herein designated VGAM GENE, encodes a VGAM210 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM210 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM210 precursor RNA is designated SEQ ID:5002, and is provided hereinbelow with reference to the sequence listing part.

[2896] VGAM210 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2897] An enzyme complex designated DICER COMPLEX, dices the VGAM210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM210 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM210 RNA is designated SEQ ID:5003, and is provided hereinbelow with reference to the sequence listing part.

[2898] VGAM210 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2899] VGAM210 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM210 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM210 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2900] The complementary binding of VGAM210 RNA, herein designated VGAM RNA, to host target binding sites on VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM210 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2901] It is appreciated that VGAM210 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM210 host target genes. The mRNA of each one of this plurality of VGAM210 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM210 RNA, herein designated VGAM RNA, and which when bound by VGAM210 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM210 host target proteins.

[2902] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM210 gene, herein designated VGAM GENE, on one or more VGAM210 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2903] It is yet further appreciated that a function of VGAM210 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM210 include diagnosis, prevention and

treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM210 correlate with, and may be deduced from, the identity of the host target genes which VGAM210 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2904] Nucleotide sequences of the VGAM210 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM210 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM210 are further described hereinbelow with reference to Table 1.

[2905] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM210 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2906] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 211 (VGAM211) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2907] VGAM211 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM211 was detected is described hereinabove with reference to Figs. 2–8.

[2908] VGAM211 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2909] VGAM211 gene, herein designated VGAM GENE, encodes a VGAM211 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM211 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM211 precursor RNA is designated SEQ ID:5060, and is provided hereinbelow with reference to the sequence listing part.

[2910] VGAM211 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM211 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2911] An enzyme complex designated DICER COMPLEX, dices the VGAM211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM211 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM211 RNA is designated SEQ ID:5061, and is provided hereinbelow with reference to the sequence listing part.

[2912] VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM211 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2913] VGAM211 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM211 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2914] The complementary binding of VGAM211 RNA, herein designated VGAM RNA, to host target binding sites on VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM211 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2915] It is appreciated that VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM211 host target genes. The mRNA of each one of this plurality of VGAM211 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM211 RNA, herein designated VGAM RNA, and which when bound by VGAM211 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM211 host target proteins.

[2916] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM211 gene, herein designated VGAM GENE, on one or more VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2917] It is yet further appreciated that a function of VGAM211 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific

functions, and accordingly utilities, of VGAM211 correlate with, and may be deduced from, the identity of the host target genes which VGAM211 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2918] Nucleotide sequences of the VGAM211 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM211 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM211 are further described hereinbelow with reference to Table 1.

[2919] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM211 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2920] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 212 (VGAM212) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[2921] VGAM212 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM212 was detected is described hereinabove with reference to Figs. 2–8.

[2922] VGAM212 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2923] VGAM212 gene, herein designated VGAM GENE, encodes a VGAM212 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM212 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM212 precursor RNA is designated SEQ ID:5069, and is provided hereinbelow with reference to the sequence listing part.

[2924] VGAM212 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM212 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2925] An enzyme complex designated DICER COMPLEX, dices the VGAM212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM212 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM212 RNA is designated SEQ ID:5070, and is provided hereinbelow with reference to the sequence listing part.

[2926] VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM212 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2927] VGAM212 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM212 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2928] The complementary binding of VGAM212 RNA, herein designated VGAM RNA, to host target binding sites on VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM212 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2929] It is appreciated that VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM212 host target genes. The mRNA of each one of this plurality of VGAM212 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM212 RNA, herein designated VGAM RNA, and which when bound by VGAM212 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM212 host target proteins.

[2930] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM212 gene, herein designated VGAM GENE, on one or more VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2931] It is yet further appreciated that a function of VGAM212 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM212 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM212 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2932] Nucleotide sequences of the VGAM212 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM212 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM212 are further described hereinbelow with reference to Table 1.

[2933] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM212 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2934] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 213 (VGAM213) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[2935] VGAM213 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM213 was detected is described hereinabove with reference to Figs. 2–8.

[2936] VGAM213 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2937] VGAM213 gene, herein designated VGAM GENE, encodes a VGAM213 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM213 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM213 precursor RNA is designated SEQ ID:5095, and is provided hereinbelow with reference to the sequence listing part.

[2938] VGAM213 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2939] An enzyme complex designated DICER COMPLEX, dices the VGAM213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM213 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM213 RNA is designated SEQ ID:5096, and is provided hereinbelow with reference to the sequence listing part.

[2940] VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2941] VGAM213 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM213 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM213 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2942] The complementary binding of VGAM213 RNA, herein designated VGAM RNA, to host target binding sites on VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM213 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2943] It is appreciated that VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM213 host target genes. The mRNA of each one of this plurality of VGAM213 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM213 RNA, herein designated VGAM RNA, and which when bound by VGAM213 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM213 host target proteins.

[2944] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM213 gene, herein designated VGAM GENE, on one or more VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2945] It is yet further appreciated that a function of VGAM213 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM213 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM213 correlate with, and may be deduced from, the identity of the

host target genes which VGAM213 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2946] Nucleotide sequences of the VGAM213 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM213 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM213 are further described hereinbelow with reference to Table 1.

[2947] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM213 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2948] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 214 (VGAM214) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2949] VGAM214 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM214 was detected is described hereinabove with reference to Figs. 2–8.

[2950] VGAM214 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2951] VGAM214 gene, herein designated VGAM GENE, encodes a VGAM214 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM214 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM214 precursor RNA is designated SEQ ID:5100, and is provided hereinbelow with reference to the sequence listing part.

[2952] VGAM214 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2953] An enzyme complex designated DICER COMPLEX, dices the VGAM214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM214 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM214 RNA is designated SEQ ID:5101, and is provided hereinbelow with reference to the sequence listing part.

[2954] VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5



untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2955] VGAM214 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM214 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM214 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2956] The complementary binding of VGAM214 RNA, herein designated VGAM RNA, to host target binding sites on VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM214 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2957] It is appreciated that VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM214 host target genes. The mRNA of each one of this plurality of VGAM214 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM214 RNA, herein designated VGAM RNA, and which when bound by VGAM214 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM214 host target proteins.

[2958] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM214 gene, herein designated VGAM GENE, on one or more VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2959] It is yet further appreciated that a function of VGAM214 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM214 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM214 correlate with, and may be deduced from, the identity of the host target genes which VGAM214 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[2960] Nucleotide sequences of the VGAM214 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM214 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM214 are further described hereinbelow with reference to Table 1.

[2961] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM214 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2962] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 215 (VGAM215) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2963] VGAM215 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM215 was detected is described hereinabove with reference to Figs. 2–8.

[2964] VGAM215 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2965] VGAM215 gene, herein designated VGAM GENE, encodes a VGAM215 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM215 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM215 precursor RNA is designated SEQ ID:5116, and is provided hereinbelow with reference to the sequence listing part.

[2966] VGAM215 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2967] An enzyme complex designated DICER COMPLEX, dices the VGAM215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM215 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM215 RNA is designated SEQ ID:5117, and is provided hereinbelow with reference to the sequence listing part.

[2968] VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2969] VGAM215 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM215 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM215 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[2970] The complementary binding of VGAM215 RNA, herein designated VGAM RNA, to host target binding sites on VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM215 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2971] It is appreciated that VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM215 host target genes. The mRNA of each one of this plurality of VGAM215 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM215 RNA, herein designated VGAM RNA, and which when bound by VGAM215 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM215 host target proteins.

[2972] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM215 gene, herein designated VGAM GENE, on one or more VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2973] It is yet further appreciated that a function of VGAM215 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM215 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM215 correlate with, and may be deduced from, the identity of the host target genes which VGAM215 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[2974] Nucleotide sequences of the VGAM215 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM215 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM215 are further described hereinbelow with reference to Table 1.

[2975] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM215 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2976] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 216 (VGAM216) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2977] VGAM216 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM216 was detected is described hereinabove with reference to Figs. 2–8.

[2978] VGAM216 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM216 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2979] VGAM216 gene, herein designated VGAM GENE, encodes a VGAM216 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM216 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM216 precursor RNA is designated SEQ ID:5218, and is provided hereinbelow with reference to the sequence listing part.

[2980] VGAM216 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2981] An enzyme complex designated DICER COMPLEX, dices the VGAM216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM216 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM216 RNA is designated SEQ ID:5219, and is provided hereinbelow with reference to the sequence listing part.

[2982] VGAM216 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[2983] VGAM216 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM216 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2984] The complementary binding of VGAM216 RNA, herein designated VGAM RNA, to host target binding sites on VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM216 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2985] It is appreciated that VGAM216 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM216 host target genes. The mRNA of each one of this plurality of VGAM216 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM216 RNA, herein designated VGAM RNA, and which when bound by VGAM216 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM216 host target proteins.

[2986] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM216 gene, herein designated VGAM GENE, on one or

more VGAM216 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[2987] It is yet further appreciated that a function of VGAM216 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM216 correlate with, and may be deduced from, the identity of the host target genes which VGAM216 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[2988] Nucleotide sequences of the VGAM216 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM216 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM216 are further described hereinbelow with reference to Table 1.

[2989] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM216 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[2990] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 217 (VGAM217) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[2991] VGAM217 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM217 was detected is described



hereinabove with reference to Figs. 2–8.

[2992] VGAM217 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM217 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[2993] VGAM217 gene, herein designated VGAM GENE, encodes a VGAM217 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM217 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM217 precursor RNA is designated SEQ ID:5247, and is provided hereinbelow with reference to the sequence listing part.

[2994] VGAM217 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[2995] An enzyme complex designated DICER COMPLEX, dices the VGAM217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM217 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM217 RNA is designated SEQ ID:5248, and is provided hereinbelow with reference to the sequence listing part.

[2996] VGAM217 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[2997] VGAM217 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM217 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[2998] The complementary binding of VGAM217 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM217 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[2999] It is appreciated that VGAM217 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM217 host target genes. The mRNA of each one of this plurality of VGAM217 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM217 RNA, herein designated VGAM RNA, and which when bound by VGAM217 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM217 host target proteins.

[3000] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM217 gene, herein designated VGAM GENE, on one or more VGAM217 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3001] It is yet further appreciated that a function of VGAM217 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM217 correlate with, and may be deduced from, the identity of the host target genes which VGAM217 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3002] Nucleotide sequences of the VGAM217 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM217 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM217 are further described hereinbelow with reference to Table 1.

[3003] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM217 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3004] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 218 (VGAM218) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3005] VGAM218 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM218 was detected is described hereinabove with reference to Figs. 2-8.

[3006] VGAM218 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3007] VGAM218 gene, herein designated VGAM GENE, encodes a VGAM218 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM218 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM218 precursor RNA is designated SEQ ID:5253, and is provided hereinbelow with reference to the sequence listing part.

[3008] VGAM218 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[3009] An enzyme complex designated DICER COMPLEX, dices the VGAM218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM218 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM218 RNA is designated SEQ ID:5254, and is provided hereinbelow with reference to the sequence listing part.

[3010] VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3011] VGAM218 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM218 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM218 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3012] The complementary binding of VGAM218 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM218 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3013] It is appreciated that VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM218 host target genes. The mRNA of each one of this plurality of VGAM218 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM218 RNA, herein designated VGAM RNA, and which when bound by VGAM218 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM218 host target proteins.

[3014] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM218 gene, herein designated VGAM GENE, on one or more VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3015] It is yet further appreciated that a function of VGAM218 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM218 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM218 correlate with, and may be deduced from, the identity of the host target genes which VGAM218 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3016] Nucleotide sequences of the VGAM218 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM218 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM218 are further described hereinbelow with reference to Table 1.

[3017] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM218 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3018] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 219 (VGAM219) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3019] VGAM219 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM219 was detected is described hereinabove with reference to Figs. 2-8.

[3020] VGAM219 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine herpesvirus 2. VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3021] VGAM219 gene, herein designated VGAM GENE, encodes a VGAM219 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM219 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM219 precursor RNA is designated SEQ ID:5270, and is provided hereinbelow with reference to the sequence listing part.

[3022] VGAM219 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3023] An enzyme complex designated DICER COMPLEX, dices the VGAM219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM219 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM219 RNA is designated SEQ ID:5271, and is provided hereinbelow with reference to the sequence listing part.

[3024] VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3025] VGAM219 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM219 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM219 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3026] The complementary binding of VGAM219 RNA, herein designated VGAM RNA, to host target binding sites on VGAM219 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM219 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3027] It is appreciated that VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM219 host target genes. The mRNA of each one of this plurality of VGAM219 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM219 RNA, herein designated VGAM RNA, and which when bound by VGAM219 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM219 host target proteins.

[3028] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM219 gene, herein designated VGAM GENE, on one or more VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3029] It is yet further appreciated that a function of VGAM219 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM219 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM219 correlate with, and may be deduced from, the identity of the host target genes which VGAM219 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3030] Nucleotide sequences of the VGAM219 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM219 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM219 are further described hereinbelow with reference to Table 1.

[3031] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM219 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3032] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 220 (VGAM220) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3033] VGAM220 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM220 was detected is described hereinabove with reference to Figs. 2-8.

[3034] VGAM220 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1.

VGAM220 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3035] VGAM220 gene, herein designated VGAM GENE, encodes a VGAM220 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM220 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM220 precursor RNA is designated SEQ ID:5277, and is provided hereinbelow with reference to the sequence listing part.

[3036] VGAM220 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3037] An enzyme complex designated DICER COMPLEX, dices

the VGAM220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM220 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM220 RNA is designated SEQ ID:5278, and is provided hereinbelow with reference to the sequence listing part.

[3038] VGAM220 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3039] VGAM220 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM220 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM220 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3040] The complementary binding of VGAM220 RNA, herein designated VGAM RNA, to host target binding sites on VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM220 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3041] It is appreciated that VGAM220 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM220 host target genes. The mRNA of each one of this plurality of VGAM220 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM220 RNA, herein designated VGAM RNA, and which when bound by VGAM220 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM220 host target proteins.

[3042] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM220 gene, herein designated VGAM GENE, on one or more VGAM220 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3043] It is yet further appreciated that a function of VGAM220 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM220 correlate with, and may be deduced from, the identity of the host target genes which VGAM220 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3044] Nucleotide sequences of the VGAM220 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM220 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM220 are further described hereinbelow with reference to Table 1.

[3045] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM220 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3046] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 221 (VGAM221) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3047] VGAM221 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM221 was detected is described hereinabove with reference to Figs. 2-8.

[3048] VGAM221 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM221 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[3049] VGAM221 gene, herein designated VGAM GENE, encodes a VGAM221 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM221 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM221 precursor RNA is designated SEQ ID:5292, and is provided hereinbelow with reference to the sequence listing part.

[3050] VGAM221 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3051] An enzyme complex designated DICER COMPLEX, dices the VGAM221 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM221 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM221 RNA is designated SEQ ID:5293, and is provided hereinbelow with reference to the sequence listing part.

[3052] VGAM221 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3053] VGAM221 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM221 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3054] The complementary binding of VGAM221 RNA, herein designated VGAM RNA, to host target binding sites on VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM221 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM221 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3055] It is appreciated that VGAM221 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM221 host target genes. The mRNA of each one of this plurality of VGAM221 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM221 RNA, herein designated VGAM RNA, and which when bound by VGAM221 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM221 host target proteins.

[3056] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM221 gene, herein designated VGAM GENE, on one or more VGAM221 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3057] It is yet further appreciated that a function of VGAM221 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM221 correlate with, and may be deduced from, the identity of the host target genes which VGAM221 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3058] Nucleotide sequences of the VGAM221 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM221 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM221 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM221 are further described hereinbelow with reference to Table 1.

[3059] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM221 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3060] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 222 (VGAM222) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3061] VGAM222 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM222 was detected is described hereinabove with reference to Figs. 2-8.

[3062] VGAM222 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[3063] VGAM222 gene, herein designated VGAM GENE, encodes a VGAM222 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM222 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM222 precursor RNA is designated SEQ ID:5296, and is provided hereinbelow with reference to the sequence listing part.

[3064] VGAM222 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3065] An enzyme complex designated DICER COMPLEX, dices the VGAM222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM222 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM222 RNA is designated SEQ ID:5297, and is provided hereinbelow with reference to the sequence listing part.

[3066] VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3067] VGAM222 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM222 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM222 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3068] The complementary binding of VGAM222 RNA, herein designated VGAM RNA, to host target binding sites on VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM222 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3069] It is appreciated that VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM222 host target genes. The mRNA of each one of this plurality of VGAM222 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM222 RNA, herein designated VGAM RNA, and which when bound by VGAM222 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM222 host target proteins.

[3070] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM222 gene, herein designated VGAM GENE, on one or more VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3071] It is yet further appreciated that a function of VGAM222 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM222 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM222 correlate with, and may be deduced from, the identity of the host target genes which VGAM222 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3072] Nucleotide sequences of the VGAM222 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM222 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM222 are further de-

scribed hereinbelow with reference to Table 1.

[3073] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM222 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3074] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 223 (VGAM223) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3075] VGAM223 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM223 was detected is described hereinabove with reference to Figs. 2-8.

[3076] VGAM223 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM223 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3077] VGAM223 gene, herein designated VGAM GENE, encodes a VGAM223 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM223 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM223 precursor RNA is designated SEQ ID:5309, and is provided hereinbelow with reference to the sequence listing part.

[3078] VGAM223 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[3079] An enzyme complex designated DICER COMPLEX, dices the VGAM223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM223 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM223 RNA is designated SEQ ID:5310, and is provided hereinbelow with reference to the sequence listing part.

[3080] VGAM223 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3081] VGAM223 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM223 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3082] The complementary binding of VGAM223 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM223 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3083] It is appreciated that VGAM223 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM223 host target genes. The mRNA of each one of this plurality of VGAM223 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM223 RNA, herein designated VGAM RNA, and which when bound by VGAM223 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM223 host target proteins.

[3084] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM223 gene, herein designated VGAM GENE, on one or more VGAM223 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3085] It is yet further appreciated that a function of VGAM223 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM223 correlate with, and may be deduced from, the identity of the host target genes which VGAM223 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3086] Nucleotide sequences of the VGAM223 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM223 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM223 are further described hereinbelow with reference to Table 1.

[3087] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM223 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3088] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 224 (VGAM224) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3089] VGAM224 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM224 was detected is described hereinabove with reference to Figs. 2-8.

[3090] VGAM224 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Chimpanzee cytomegalovirus. VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3091] VGAM224 gene, herein designated VGAM GENE, encodes a VGAM224 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM224 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM224 precursor RNA is designated SEQ ID:5332, and is provided hereinbelow with reference to the sequence listing part.

[3092] VGAM224 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3093] An enzyme complex designated DICER COMPLEX, dices the VGAM224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM224 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM224 RNA is designated SEQ ID:5333, and is provided hereinbelow with reference to the sequence listing part.

[3094] VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3095] VGAM224 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM224 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM224 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3096] The complementary binding of VGAM224 RNA, herein designated VGAM RNA, to host target binding sites on VGAM224 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM224 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3097] It is appreciated that VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM224 host target genes. The mRNA of each one of this plurality of VGAM224 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM224 RNA, herein designated VGAM RNA, and which when bound by VGAM224 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM224 host target proteins.

[3098] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM224 gene, herein designated VGAM GENE, on one or more VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3099] It is yet further appreciated that a function of VGAM224 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM224 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM224 correlate with, and may be deduced from, the identity of the host target genes which VGAM224 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3100] Nucleotide sequences of the VGAM224 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM224 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM224 are further described hereinbelow with reference to Table 1.

[3101] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM224 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3102] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 225 (VGAM225) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3103] VGAM225 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM225 was detected is described hereinabove with reference to Figs. 2-8.

[3104] VGAM225 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.



VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3105] VGAM225 gene, herein designated VGAM GENE, encodes a VGAM225 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM225 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM225 precursor RNA is designated SEQ ID:5348, and is provided hereinbelow with reference to the sequence listing part.

[3106] VGAM225 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3107] An enzyme complex designated DICER COMPLEX, dices

the VGAM225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM225 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM225 RNA is designated SEQ ID:5349, and is provided hereinbelow with reference to the sequence listing part.

[3108] VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3109] VGAM225 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM225 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM225 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM225 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3110] The complementary binding of VGAM225 RNA, herein designated VGAM RNA, to host target binding sites on VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM225 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3111] It is appreciated that VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM225 host target genes. The mRNA of each one of this plurality of VGAM225 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM225 RNA, herein designated VGAM RNA, and which when bound by VGAM225 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM225 host target proteins.

[3112] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM225 gene, herein designated VGAM GENE, on one or more VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3113] It is yet further appreciated that a function of VGAM225 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM225 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM225 correlate with, and may be deduced from, the identity of the host target genes which VGAM225 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3114] Nucleotide sequences of the VGAM225 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM225 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM225 are further described hereinbelow with reference to Table 1.

[3115] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM225 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3116] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 226 (VGAM226) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3117] VGAM226 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM226 was detected is described hereinabove with reference to Figs. 2-8.

[3118] VGAM226 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM226 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[3119] VGAM226 gene, herein designated VGAM GENE, encodes a VGAM226 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM226 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM226 precursor RNA is designated SEQ ID:5358, and is provided hereinbelow with reference to the sequence listing part.

[3120] VGAM226 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3121] An enzyme complex designated DICER COMPLEX, dices the VGAM226 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM226 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM226 RNA is designated SEQ ID:5359, and is provided hereinbelow with reference to the sequence listing part.

[3122] VGAM226 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3123] VGAM226 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM226 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM226 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3124] The complementary binding of VGAM226 RNA, herein designated VGAM RNA, to host target binding sites on VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM226 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM226 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3125] It is appreciated that VGAM226 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM226 host target genes. The mRNA of each one of this plurality of VGAM226 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM226 RNA, herein designated VGAM RNA, and which when bound by VGAM226 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM226 host target proteins.

[3126] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM226 gene, herein designated VGAM GENE, on one or more VGAM226 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3127] It is yet further appreciated that a function of VGAM226 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM226 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM226 correlate with, and may be deduced from, the identity of the host target genes which VGAM226 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3128] Nucleotide sequences of the VGAM226 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM226 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM226 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM226 are further described hereinbelow with reference to Table 1.

[3129] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM226 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3130] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 227 (VGAM227) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3131] VGAM227 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM227 was detected is described hereinabove with reference to Figs. 2-8.

[3132] VGAM227 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[3133] VGAM227 gene, herein designated VGAM GENE, encodes a VGAM227 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM227 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM227 precursor RNA is designated SEQ ID:5362, and is provided hereinbelow with reference to the sequence listing part.

[3134] VGAM227 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3135] An enzyme complex designated DICER COMPLEX, dices the VGAM227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM227 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM227 RNA is designated SEQ ID:5363, and is provided hereinbelow with reference to the sequence listing part.

[3136] VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3137] VGAM227 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM227 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM227 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3138] The complementary binding of VGAM227 RNA, herein designated VGAM RNA, to host target binding sites on VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM227 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3139] It is appreciated that VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM227 host target genes. The mRNA of each one of this plurality of VGAM227 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM227 RNA, herein designated VGAM RNA, and which when bound by VGAM227 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM227 host target proteins.

[3140] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM227 gene, herein designated VGAM GENE, on one or more VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3141] It is yet further appreciated that a function of VGAM227 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM227 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM227 correlate with, and may be deduced from, the identity of the host target genes which VGAM227 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3142] Nucleotide sequences of the VGAM227 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM227 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM227 are further de-

scribed hereinbelow with reference to Table 1.

[3143] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM227 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3144] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 228 (VGAM228) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3145] VGAM228 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM228 was detected is described hereinabove with reference to Figs. 2-8.

[3146] VGAM228 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3147] VGAM228 gene, herein designated VGAM GENE, encodes a VGAM228 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM228 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM228 precursor RNA is designated SEQ ID:5381, and is provided hereinbelow with reference to the sequence listing part.

[3148] VGAM228 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3149] An enzyme complex designated DICER COMPLEX, dices the VGAM228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM228 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM228 RNA is designated SEQ ID:5382, and is provided hereinbelow with reference to the sequence listing part.

[3150] VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3151] VGAM228 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM228 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM228 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3152] The complementary binding of VGAM228 RNA, herein designated VGAM RNA, to host target binding sites on VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM228 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3153] It is appreciated that VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM228 host target genes. The mRNA of each one of this plurality of VGAM228 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM228 RNA, herein designated VGAM RNA, and which when bound by VGAM228 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM228 host target proteins.

[3154] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM228 gene, herein designated VGAM GENE, on one or more VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3155] It is yet further appreciated that a function of VGAM228 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM228 correlate with, and may be deduced from, the identity of the host target genes which VGAM228 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3156] Nucleotide sequences of the VGAM228 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM228 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM228 are further described hereinbelow with reference to Table 1.

[3157] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM228 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3158] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 229 (VGAM229) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3159] VGAM229 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM229 was detected is described hereinabove with reference to Figs. 2-8.

[3160] VGAM229 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3161] VGAM229 gene, herein designated VGAM GENE, encodes a



VGAM229 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM229 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM229 precursor RNA is designated SEQ ID:5433, and is provided hereinbelow with reference to the sequence listing part.

[3162] VGAM229 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3163] An enzyme complex designated DICER COMPLEX, dices the VGAM229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM229 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM229 RNA is designated SEQ ID:5434, and is provided hereinbelow with reference to the sequence listing part.

[3164] VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3165] VGAM229 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM229 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3166] The complementary binding of VGAM229 RNA, herein designated VGAM RNA, to host target binding sites on VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM229 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[3167] It is appreciated that VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM229 host target genes. The mRNA of each one of this plurality of VGAM229 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM229 RNA, herein designated VGAM RNA, and which when bound by VGAM229 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM229 host target proteins.

[3168] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM229 gene, herein designated VGAM GENE, on one or more VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3169] It is yet further appreciated that a function of VGAM229 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM229 correlate with, and may be deduced from, the identity of the host target genes which VGAM229 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3170] Nucleotide sequences of the VGAM229 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM229 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM229 are further described hereinbelow with reference to Table 1.

[3171] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM229 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3172] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 230 (VGAM230) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3173] VGAM230 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM230 was detected is described hereinabove with reference to Figs. 2-8.

[3174] VGAM230 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM230 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3175] VGAM230 gene, herein designated VGAM GENE, encodes a VGAM230 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM230 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM230 precursor RNA is designated SEQ ID:5437, and is provided hereinbelow with reference to the sequence listing part.

[3176] VGAM230 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3177] An enzyme complex designated DICER COMPLEX, dices the VGAM230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM230 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM230 RNA is designated SEQ ID:5438, and is provided hereinbelow with reference to the sequence listing part.

[3178] VGAM230 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3179] VGAM230 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host



target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM230 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3180] The complementary binding of VGAM230 RNA, herein designated VGAM RNA, to host target binding sites on VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM230 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3181] It is appreciated that VGAM230 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM230 host target genes. The mRNA of each one of this plurality of VGAM230 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM230 RNA, herein designated VGAM RNA, and which when bound by VGAM230 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM230 host target proteins.

[3182] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM230 gene, herein designated VGAM GENE, on one or more VGAM230 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3183] It is yet further appreciated that a function of VGAM230 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM230 correlate with, and may be deduced from, the identity of the host target genes which VGAM230 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3184] Nucleotide sequences of the VGAM230 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM230 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM230 are further described hereinbelow with reference to Table 1.

[3185] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM230 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3186] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 231 (VGAM231) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3187] VGAM231 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM231 was detected is described hereinabove with reference to Figs. 2–8.

[3188] VGAM231 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM231 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3189] VGAM231 gene, herein designated VGAM GENE, encodes a VGAM231 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM231 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM231 precursor RNA is designated SEQ ID:5446, and is provided hereinbelow with reference to the sequence listing part.

[3190] VGAM231 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3191] An enzyme complex designated DICER COMPLEX, dices the VGAM231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM231 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM231 RNA is designated SEQ ID:5447, and is provided hereinbelow with reference to the sequence listing part.

[3192] VGAM231 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3193] VGAM231 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM231 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3194] The complementary binding of VGAM231 RNA, herein designated VGAM RNA, to host target binding sites on VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM231 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3195] It is appreciated that VGAM231 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM231 host target genes. The mRNA of each one of this plurality of VGAM231 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM231 RNA, herein designated VGAM RNA, and which when bound by VGAM231 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM231 host target proteins.

[3196] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM231 gene, herein designated VGAM GENE, on one or more VGAM231 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3197] It is yet further appreciated that a function of VGAM231 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM231 correlate with, and may be deduced from, the identity of the host target genes which VGAM231 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3198] Nucleotide sequences of the VGAM231 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM231 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM231 are further described hereinbelow with reference to Table 1.

[3199] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM231 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3200] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 232 (VGAM232) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3201] VGAM232 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM232 was detected is described hereinabove with reference to Figs. 2–8.

[3202] VGAM232 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3203] VGAM232 gene, herein designated VGAM GENE, encodes a VGAM232 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM232 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM232 precursor RNA is designated SEQ ID:5456, and is provided hereinbelow with reference to the sequence listing part.

[3204] VGAM232 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3205] An enzyme complex designated DICER COMPLEX, dices the VGAM232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM232 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM232 RNA is designated SEQ ID:5457, and is provided hereinbelow with reference to the sequence listing part.

[3206] VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3207] VGAM232 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM232 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3208] The complementary binding of VGAM232 RNA, herein designated VGAM RNA, to host target binding sites on VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM232 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3209] It is appreciated that VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM232 host target genes. The mRNA of each one of this plurality of VGAM232 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM232 RNA, herein designated VGAM RNA, and which when bound by VGAM232 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM232 host target proteins.

[3210] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM232 gene, herein designated VGAM GENE, on one or more VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[3211] It is yet further appreciated that a function of VGAM232 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM232 correlate with, and may be deduced from, the identity of the host target genes which VGAM232 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[3212] Nucleotide sequences of the VGAM232 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM232 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM232 are further described hereinbelow with reference to Table 1.

[3213] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM232 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3214] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 233 (VGAM233) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3215] VGAM233 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM233 was detected is described hereinabove with reference to Figs. 2–8.

[3216] VGAM233 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Transmissible gastroenteritis virus. VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3217] VGAM233 gene, herein designated VGAM GENE, encodes a VGAM233 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM233 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a



protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM233 precursor RNA is designated SEQ ID:5474, and is provided hereinbelow with reference to the sequence listing part.

[3218] VGAM233 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3219] An enzyme complex designated DICER COMPLEX, dices the VGAM233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM233 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM233 RNA is designated SEQ ID:5475, and is provided hereinbelow with reference to the sequence listing part.

[3220] VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3221] VGAM233 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM233 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3222] The complementary binding of VGAM233 RNA, herein designated VGAM RNA, to host target binding sites on VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM233 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3223] It is appreciated that VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM233 host target genes. The mRNA of

each one of this plurality of VGAM233 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM233 RNA, herein designated VGAM RNA, and which when bound by VGAM233 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM233 host target proteins.

[3224] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM233 gene, herein designated VGAM GENE, on one or more VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[3225] It is yet further appreciated that a function of VGAM233 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of viral infection by Transmissible gastroenteritis virus. Specific functions, and accordingly utilities, of VGAM233 correlate with, and may be deduced from, the identity of the host target genes which VGAM233 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3226] Nucleotide sequences of the VGAM233 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM233 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM233 are further described hereinbelow with reference to Table 1.

[3227] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM233 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[3228] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 234 (VGAM234) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3229] VGAM234 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM234 was detected is described hereinabove with reference to Figs. 2–8.

[3230] VGAM234 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3231] VGAM234 gene, herein designated VGAM GENE, encodes a VGAM234 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM234 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM234 precursor RNA is designated SEQ ID:5504, and is provided hereinbelow with reference to the sequence listing part.

[3232] VGAM234 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3233] An enzyme complex designated DICER COMPLEX, dices the VGAM234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM234 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM234 RNA is designated SEQ ID:5505, and

is provided hereinbelow with reference to the sequence listing part.

[3234] VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3235] VGAM234 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM234 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3236] The complementary binding of VGAM234 RNA, herein designated VGAM RNA, to host target binding sites on VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM234 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3237] It is appreciated that VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM234 host target genes. The mRNA of each one of this plurality of VGAM234 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM234 RNA, herein designated VGAM RNA, and which when bound by VGAM234 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM234 host target proteins.

[3238] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM234 gene, herein designated VGAM GENE, on one or more VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3239] It is yet further appreciated that a function of VGAM234 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM234 correlate with, and may be deduced from, the identity of the host target genes which VGAM234 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3240] Nucleotide sequences of the VGAM234 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM234 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM234 are further described hereinbelow with reference to Table 1.

[3241] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM234 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3242] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 235 (VGAM235) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3243] VGAM235 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM235 was detected is described hereinabove with reference to Figs. 2–8.

[3244] VGAM235 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3245] VGAM235 gene, herein designated VGAM GENE, encodes a VGAM235 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM235 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM235 precursor RNA is

designated SEQ ID:5625, and is provided hereinbelow with reference to the sequence listing part.

[3246] VGAM235 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3247] An enzyme complex designated DICER COMPLEX, dices the VGAM235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM235 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM235 RNA is designated SEQ ID:5626, and is provided hereinbelow with reference to the sequence

listing part.

[3248] VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3249] VGAM235 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM235 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3250] The complementary binding of VGAM235 RNA, herein designated VGAM RNA, to host target binding sites on VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM235 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3251] It is appreciated that VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM235 host target genes. The mRNA of each one of this plurality of VGAM235 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM235 RNA, herein designated VGAM RNA, and which when bound by VGAM235 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM235 host target proteins.

[3252] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM235 gene, herein designated VGAM GENE, on one or more VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3253] It is yet further appreciated that a function of VGAM235 is



inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM235 correlate with, and may be deduced from, the identity of the host target genes which VGAM235 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3254] Nucleotide sequences of the VGAM235 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM235 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM235 are further described hereinbelow with reference to Table 1.

[3255] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM235 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3256] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 236 (VGAM236) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3257] VGAM236 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM236 was detected is described hereinabove with reference to Figs. 2–8.

[3258] VGAM236 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3259] VGAM236 gene, herein designated VGAM GENE, encodes a VGAM236 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM236 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM236 precursor RNA is designated SEQ ID:5630, and is provided hereinbelow with

reference to the sequence listing part.

[3260] VGAM236 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3261] An enzyme complex designated DICER COMPLEX, dices the VGAM236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM236 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM236 RNA is designated SEQ ID:5631, and is provided hereinbelow with reference to the sequence listing part.

[3262] VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3263] VGAM236 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM236 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3264] The complementary binding of VGAM236 RNA, herein designated VGAM RNA, to host target binding sites on VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM236 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3265] It is appreciated that VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM236 host target genes. The mRNA of each one of this plurality of VGAM236 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM236 RNA, herein designated VGAM RNA, and which when bound by VGAM236 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM236 host target proteins.

[3266] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM236 gene, herein designated VGAM GENE, on one or more VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3267] It is yet further appreciated that a function of VGAM236 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM236 correlate with, and may be deduced from, the identity of the host target genes which VGAM236 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3268] Nucleotide sequences of the VGAM236 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM236 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM236 are further described hereinbelow with reference to Table 1.

[3269] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM236 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3270] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 237 (VGAM237) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3271] VGAM237 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM237 was detected is described hereinabove with reference to Figs. 2–8.

[3272] VGAM237 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM237 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3273] VGAM237 gene, herein designated VGAM GENE, encodes a VGAM237 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM237 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM237 precursor RNA is designated SEQ ID:5636, and is provided hereinbelow with reference to the sequence listing part.



[3274] VGAM237 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3275] An enzyme complex designated DICER COMPLEX, dices the VGAM237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM237 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM237 RNA is designated SEQ ID:5637, and is provided hereinbelow with reference to the sequence listing part.

[3276] VGAM237 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3277] VGAM237 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM237 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM237 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3278] The complementary binding of VGAM237 RNA, herein designated VGAM RNA, to host target binding sites on VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM237 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3279] It is appreciated that VGAM237 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM237 host target genes. The mRNA of each one of this plurality of VGAM237 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM237 RNA, herein designated VGAM

RNA, and which when bound by VGAM237 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM237 host target proteins.

[3280] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM237 gene, herein designated VGAM GENE, on one or more VGAM237 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3281] It is yet further appreciated that a function of VGAM237 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM237 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM237 correlate with, and may be deduced from, the identity of the host target genes which VGAM237 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3282] Nucleotide sequences of the VGAM237 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM237 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM237 are further described hereinbelow with reference to Table 1.

[3283] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM237 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3284] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 238 (VGAM238) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3285] VGAM238 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM238 was detected is described hereinabove with reference to Figs. 2–8.

[3286] VGAM238 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Transmissible gastroenteritis virus. VGAM238 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3287] VGAM238 gene, herein designated VGAM GENE, encodes a VGAM238 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM238 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM238 precursor RNA is designated SEQ ID:5640, and is provided hereinbelow with reference to the sequence listing part.

[3288] VGAM238 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3289] An enzyme complex designated DICER COMPLEX, dices the VGAM238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM238 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM238 RNA is designated SEQ ID:5641, and is provided hereinbelow with reference to the sequence listing part.

[3290] VGAM238 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3291] VGAM238 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM238 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM238 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM238 host



target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3292] The complementary binding of VGAM238 RNA, herein designated VGAM RNA, to host target binding sites on VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM238 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3293] It is appreciated that VGAM238 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM238 host target genes. The mRNA of each one of this plurality of VGAM238 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM238 RNA, herein designated VGAM RNA, and which when bound by VGAM238 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM238 host target proteins.

[3294] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM238 gene, herein designated VGAM GENE, on one or more VGAM238 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3295] It is yet further appreciated that a function of VGAM238 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM238 include diagnosis, prevention and

treatment of viral infection by Transmissible gastroenteritis virus. Specific functions, and accordingly utilities, of VGAM238 correlate with, and may be deduced from, the identity of the host target genes which VGAM238 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3296] Nucleotide sequences of the VGAM238 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM238 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM238 are further described hereinbelow with reference to Table 1.

[3297] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM238 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3298] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 239 (VGAM239) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3299] VGAM239 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM239 was detected is described hereinabove with reference to Figs. 2–8.

[3300] VGAM239 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM239 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3301] VGAM239 gene, herein designated VGAM GENE, encodes a VGAM239 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM239 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM239 precursor RNA is designated SEQ ID:5647, and is provided hereinbelow with reference to the sequence listing part.

[3302] VGAM239 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM239 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3303] An enzyme complex designated DICER COMPLEX, dices the VGAM239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM239 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM239 RNA is designated SEQ ID:5648, and is provided hereinbelow with reference to the sequence listing part.

[3304] VGAM239 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM239 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3305] VGAM239 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM239 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM239 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3306] The complementary binding of VGAM239 RNA, herein designated VGAM RNA, to host target binding sites on VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM239 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3307] It is appreciated that VGAM239 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM239 host target genes. The mRNA of each one of this plurality of VGAM239 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM239 RNA, herein designated VGAM RNA, and which when bound by VGAM239 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM239 host target proteins.

[3308] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM239 gene, herein designated VGAM GENE, on one or more VGAM239 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3309] It is yet further appreciated that a function of VGAM239 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of viral infection by Chimpanzee cy-



tomegalovirus. Specific functions, and accordingly utilities, of VGAM239 correlate with, and may be deduced from, the identity of the host target genes which VGAM239 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3310] Nucleotide sequences of the VGAM239 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM239 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM239 are further described hereinbelow with reference to Table 1.

[3311] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM239 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3312] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 240 (VGAM240) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[3313] VGAM240 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM240 was detected is described hereinabove with reference to Figs. 2–8.

[3314] VGAM240 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM240 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3315] VGAM240 gene, herein designated VGAM GENE, encodes a VGAM240 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM240 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM240 precursor RNA is designated SEQ ID:5766, and is provided hereinbelow with reference to the sequence listing part.

[3316] VGAM240 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM240 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3317] An enzyme complex designated DICER COMPLEX, dices the VGAM240 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM240 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM240 RNA is designated SEQ ID:5767, and is provided hereinbelow with reference to the sequence listing part.

[3318] VGAM240 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM240 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3319] VGAM240 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM240 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM240 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3320] The complementary binding of VGAM240 RNA, herein designated VGAM RNA, to host target binding sites on VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM240 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3321] It is appreciated that VGAM240 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM240 host target genes. The mRNA of each one of this plurality of VGAM240 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM240 RNA, herein designated VGAM RNA, and which when bound by VGAM240 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM240 host target proteins.

[3322] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM240 gene, herein designated VGAM GENE, on one or more VGAM240 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3323] It is yet further appreciated that a function of VGAM240 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM240 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utili-

ties, of VGAM240 correlate with, and may be deduced from, the identity of the host target genes which VGAM240 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3324] Nucleotide sequences of the VGAM240 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM240 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM240 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM240 are further described hereinbelow with reference to Table 1.

[3325] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM240 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3326] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 241 (VGAM241) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[3327] VGAM241 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM241 was detected is described hereinabove with reference to Figs. 2–8.

[3328] VGAM241 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3329] VGAM241 gene, herein designated VGAM GENE, encodes a VGAM241 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM241 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM241 precursor RNA is designated SEQ ID:5799, and is provided hereinbelow with reference to the sequence listing part.

[3330] VGAM241 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.



As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3331] An enzyme complex designated DICER COMPLEX, dices the VGAM241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM241 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM241 RNA is designated SEQ ID:5800, and is provided hereinbelow with reference to the sequence listing part.

[3332] VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3333] VGAM241 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM241 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3334] The complementary binding of VGAM241 RNA, herein designated VGAM RNA, to host target binding sites on VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM241 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3335] It is appreciated that VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM241 host target genes. The mRNA of each one of this plurality of VGAM241 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM241 RNA, herein designated VGAM RNA, and which when bound by VGAM241 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM241 host target proteins.

[3336] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM241 gene, herein designated VGAM GENE, on one or more VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3337] It is yet further appreciated that a function of VGAM241 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM241 correlate with, and may be deduced

from, the identity of the host target genes which VGAM241 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3338] Nucleotide sequences of the VGAM241 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM241 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM241 are further described hereinbelow with reference to Table 1.

[3339] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM241 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3340] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 242 (VGAM242) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3341] VGAM242 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM242 was detected is described hereinabove with reference to Figs. 2–8.

[3342] VGAM242 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM242 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3343] VGAM242 gene, herein designated VGAM GENE, encodes a VGAM242 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM242 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM242 precursor RNA is designated SEQ ID:6450, and is provided hereinbelow with reference to the sequence listing part.

[3344] VGAM242 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3345] An enzyme complex designated DICER COMPLEX, dices the VGAM242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM242 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM242 RNA is designated SEQ ID:6451, and is provided hereinbelow with reference to the sequence listing part.

[3346] VGAM242 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3347] VGAM242 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM242 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-



cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3348] The complementary binding of VGAM242 RNA, herein designated VGAM RNA, to host target binding sites on VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM242 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3349] It is appreciated that VGAM242 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM242 host target genes. The mRNA of each one of this plurality of VGAM242 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM242 RNA, herein designated VGAM RNA, and which when bound by VGAM242 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM242 host target proteins.

[3350] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM242 gene, herein designated VGAM GENE, on one or more VGAM242 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3351] It is yet further appreciated that a function of VGAM242 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM242 correlate with, and may be deduced from, the identity of the host target genes which VGAM242 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[3352] Nucleotide sequences of the VGAM242 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM242 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM242 are further described hereinbelow with reference to Table 1.

[3353] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM242 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3354] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 243 (VGAM243) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3355] VGAM243 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM243 was detected is described hereinabove with reference to Figs. 2–8.

[3356] VGAM243 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3357] VGAM243 gene, herein designated VGAM GENE, encodes a VGAM243 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM243 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM243 precursor RNA is designated SEQ ID:6472, and is provided hereinbelow with reference to the sequence listing part.

[3358] VGAM243 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3359] An enzyme complex designated DICER COMPLEX, dices the VGAM243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM243 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM243 RNA is designated SEQ ID:6473, and is provided hereinbelow with reference to the sequence listing part.

[3360] VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3361] VGAM243 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM243 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[3362] The complementary binding of VGAM243 RNA, herein designated VGAM RNA, to host target binding sites on VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM243 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3363] It is appreciated that VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM243 host target genes. The mRNA of each one of this plurality of VGAM243 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM243 RNA, herein designated VGAM RNA, and which when bound by VGAM243 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM243 host target proteins.

[3364] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM243 gene, herein designated VGAM GENE, on one or more VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3365] It is yet further appreciated that a function of VGAM243 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM243 correlate with, and may be deduced from, the identity of the host target genes which VGAM243 binds and inhibits, and the function of these host target genes, as elaborated



hereinbelow.

[3366] Nucleotide sequences of the VGAM243 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM243 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM243 are further described hereinbelow with reference to Table 1.

[3367] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM243 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3368] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 244 (VGAM244) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3369] VGAM244 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM244 was detected is described hereinabove with reference to Figs. 2–8.

[3370] VGAM244 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM244 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3371] VGAM244 gene, herein designated VGAM GENE, encodes a VGAM244 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM244 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM244 precursor RNA is designated SEQ ID:6480, and is provided hereinbelow with reference to the sequence listing part.

[3372] VGAM244 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3373] An enzyme complex designated DICER COMPLEX, dices the VGAM244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM244 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM244 RNA is designated SEQ ID:6481, and is provided hereinbelow with reference to the sequence listing part.

[3374] VGAM244 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[3375] VGAM244 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM244 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM244 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3376] The complementary binding of VGAM244 RNA, herein designated VGAM RNA, to host target binding sites on VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM244 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3377] It is appreciated that VGAM244 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM244 host target genes. The mRNA of each one of this plurality of VGAM244 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM244 RNA, herein designated VGAM RNA, and which when bound by VGAM244 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM244 host target proteins.

[3378] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM244 gene, herein designated VGAM GENE, on one or

more VGAM244 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3379] It is yet further appreciated that a function of VGAM244 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM244 correlate with, and may be deduced from, the identity of the host target genes which VGAM244 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3380] Nucleotide sequences of the VGAM244 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM244 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM244 are further described hereinbelow with reference to Table 1.

[3381] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM244 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3382] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 245 (VGAM245) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3383] VGAM245 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM245 was detected is described

hereinabove with reference to Figs. 2–8.

[3384] VGAM245 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM245 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3385] VGAM245 gene, herein designated VGAM GENE, encodes a VGAM245 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM245 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM245 precursor RNA is designated SEQ ID:6496, and is provided hereinbelow with reference to the sequence listing part.

[3386] VGAM245 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3387] An enzyme complex designated DICER COMPLEX, dices the VGAM245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM245 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM245 RNA is designated SEQ ID:6497, and is provided hereinbelow with reference to the sequence listing part.

[3388] VGAM245 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3389] VGAM245 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM245 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3390] The complementary binding of VGAM245 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM245 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3391] It is appreciated that VGAM245 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM245 host target genes. The mRNA of each one of this plurality of VGAM245 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM245 RNA, herein designated VGAM RNA, and which when bound by VGAM245 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM245 host target proteins.

[3392] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM245 gene, herein designated VGAM GENE, on one or more VGAM245 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3393] It is yet further appreciated that a function of VGAM245 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM245 correlate with, and may be deduced from, the identity of the host target genes which VGAM245 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3394] Nucleotide sequences of the VGAM245 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM245 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM245 are further described hereinbelow with reference to Table 1.

[3395] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM245 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3396] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 246 (VGAM246) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3397] VGAM246 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM246 was detected is described hereinabove with reference to Figs. 2-8.

[3398] VGAM246 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Transmissible gastroenteritis virus. VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3399] VGAM246 gene, herein designated VGAM GENE, encodes a VGAM246 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM246 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM246 precursor RNA is designated SEQ ID:6502, and is provided hereinbelow with reference to the sequence listing part.

[3400] VGAM246 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[3401] An enzyme complex designated DICER COMPLEX, dices the VGAM246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM246 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM246 RNA is designated SEQ ID:6503, and is provided hereinbelow with reference to the sequence listing part.

[3402] VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3403] VGAM246 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM246 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3404] The complementary binding of VGAM246 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM246 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3405] It is appreciated that VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM246 host target genes. The mRNA of each one of this plurality of VGAM246 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM246 RNA, herein designated VGAM RNA, and which when bound by VGAM246 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM246 host target proteins.

[3406] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM246 gene, herein designated VGAM GENE, on one or more VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3407] It is yet further appreciated that a function of VGAM246 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of viral infection by Transmissible gastroenteritis virus. Specific functions, and accordingly utilities, of VGAM246 correlate with, and may be deduced from, the identity of the host target genes which VGAM246 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3408] Nucleotide sequences of the VGAM246 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM246 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM246 are further described hereinbelow with reference to Table 1.

[3409] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM246 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3410] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 247 (VGAM247) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3411] VGAM247 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM247 was detected is described hereinabove with reference to Figs. 2-8.

[3412] VGAM247 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Chimpanzee cytomegalovirus. VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3413] VGAM247 gene, herein designated VGAM GENE, encodes a VGAM247 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM247 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM247 precursor RNA is designated SEQ ID:6515, and is provided hereinbelow with reference to the sequence listing part.

[3414] VGAM247 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

- [3415] An enzyme complex designated DICER COMPLEX, dices the VGAM247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM247 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM247 RNA is designated SEQ ID:6516, and is provided hereinbelow with reference to the sequence listing part.
- [3416] VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.
- [3417] VGAM247 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM247 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3418] The complementary binding of VGAM247 RNA, herein designated VGAM RNA, to host target binding sites on VGAM247 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM247 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3419] It is appreciated that VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM247 host target genes. The mRNA of each one of this plurality of VGAM247 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM247 RNA, herein designated VGAM RNA, and which when bound by VGAM247 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM247 host target proteins.

[3420] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM247 gene, herein designated VGAM GENE, on one or more VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3421] It is yet further appreciated that a function of VGAM247 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM247 correlate with, and may be deduced from, the identity of the host target genes which VGAM247 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3422] Nucleotide sequences of the VGAM247 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM247 RNA, herein designated VGAM RNA, and a



schematic representation of the secondary folding of VGAM247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM247 are further described hereinbelow with reference to Table 1.

[3423] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM247 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3424] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 248 (VGAM248) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3425] VGAM248 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM248 was detected is described hereinabove with reference to Figs. 2-8.

[3426] VGAM248 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Transmissible gastroen-

teritis virus. VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3427] VGAM248 gene, herein designated VGAM GENE, encodes a VGAM248 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM248 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM248 precursor RNA is designated SEQ ID:6529, and is provided hereinbelow with reference to the sequence listing part.

[3428] VGAM248 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3429] An enzyme complex designated DICER COMPLEX, dices

the VGAM248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM248 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM248 RNA is designated SEQ ID:6530, and is provided hereinbelow with reference to the sequence listing part.

[3430] VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3431] VGAM248 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM248 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM248 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3432] The complementary binding of VGAM248 RNA, herein designated VGAM RNA, to host target binding sites on VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM248 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3433] It is appreciated that VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM248 host target genes. The mRNA of each one of this plurality of VGAM248 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM248 RNA, herein designated VGAM RNA, and which when bound by VGAM248 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM248 host target proteins.

[3434] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM248 gene, herein designated VGAM GENE, on one or more VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3435] It is yet further appreciated that a function of VGAM248 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of viral infection by Transmissible gastroenteritis virus. Specific functions, and accordingly utilities, of VGAM248 correlate with, and may be deduced from, the identity of the host target genes which VGAM248 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3436] Nucleotide sequences of the VGAM248 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM248 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM248 are further described hereinbelow with reference to Table 1.

[3437] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM248 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3438] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 249 (VGAM249) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3439] VGAM249 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM249 was detected is described hereinabove with reference to Figs. 2-8.

[3440] VGAM249 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM249 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[3441] VGAM249 gene, herein designated VGAM GENE, encodes a VGAM249 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM249 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM249 precursor RNA is designated SEQ ID:6542, and is provided hereinbelow with reference to the sequence listing part.

[3442] VGAM249 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3443] An enzyme complex designated DICER COMPLEX, dices the VGAM249 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM249 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM249 RNA is designated SEQ ID:6543, and is provided hereinbelow with reference to the sequence listing part.

[3444] VGAM249 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3445] VGAM249 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM249 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM249 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3446] The complementary binding of VGAM249 RNA, herein designated VGAM RNA, to host target binding sites on VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM249 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM249 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3447] It is appreciated that VGAM249 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM249 host target genes. The mRNA of each one of this plurality of VGAM249 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM249 RNA, herein designated VGAM RNA, and which when bound by VGAM249 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM249 host target proteins.

[3448] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM249 gene, herein designated VGAM GENE, on one or more VGAM249 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3449] It is yet further appreciated that a function of VGAM249 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM249 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM249 correlate with, and may be deduced from, the identity of the host target genes which VGAM249 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3450] Nucleotide sequences of the VGAM249 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM249 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM249 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM249 are further described hereinbelow with reference to Table 1.

[3451] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM249 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3452] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 250 (VGAM250) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3453] VGAM250 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM250 was detected is described hereinabove with reference to Figs. 2-8.

[3454] VGAM250 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[3455] VGAM250 gene, herein designated VGAM GENE, encodes a VGAM250 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM250 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM250 precursor RNA is designated SEQ ID:6549, and is provided hereinbelow with reference to the sequence listing part.

[3456] VGAM250 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3457] An enzyme complex designated DICER COMPLEX, dices the VGAM250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM250 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM250 RNA is designated SEQ ID:6550, and is provided hereinbelow with reference to the sequence listing part.

[3458] VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3459] VGAM250 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM250 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM250 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3460] The complementary binding of VGAM250 RNA, herein designated VGAM RNA, to host target binding sites on VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA,



into VGAM250 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3461] It is appreciated that VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM250 host target genes. The mRNA of each one of this plurality of VGAM250 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM250 RNA, herein designated VGAM RNA, and which when bound by VGAM250 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM250 host target proteins.

[3462] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM250 gene, herein designated VGAM GENE, on one or more VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3463] It is yet further appreciated that a function of VGAM250 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM250 correlate with, and may be deduced from, the identity of the host target genes which VGAM250 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3464] Nucleotide sequences of the VGAM250 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM250 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM250 are further de-

scribed hereinbelow with reference to Table 1.

[3465] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM250 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3466] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 251 (VGAM251) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3467] VGAM251 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM251 was detected is described hereinabove with reference to Figs. 2-8.

[3468] VGAM251 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3469] VGAM251 gene, herein designated VGAM GENE, encodes a VGAM251 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM251 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM251 precursor RNA is designated SEQ ID:6564, and is provided hereinbelow with reference to the sequence listing part.

[3470] VGAM251 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3471] An enzyme complex designated DICER COMPLEX, dices the VGAM251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM251 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM251 RNA is designated SEQ ID:6565, and is provided hereinbelow with reference to the sequence listing part.

[3472] VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3473] VGAM251 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM251 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM251 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3474] The complementary binding of VGAM251 RNA, herein designated VGAM RNA, to host target binding sites on VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM251 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3475] It is appreciated that VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM251 host target genes. The mRNA of each one of this plurality of VGAM251 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM251 RNA, herein designated VGAM RNA, and which when bound by VGAM251 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM251 host target proteins.

[3476] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM251 gene, herein designated VGAM GENE, on one or more VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3477] It is yet further appreciated that a function of VGAM251 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM251 correlate with, and may be deduced from, the identity of the host target genes which VGAM251 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3478] Nucleotide sequences of the VGAM251 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM251 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM251 are further described hereinbelow with reference to Table 1.



[3479] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM251 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3480] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 252 (VGAM252) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3481] VGAM252 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM252 was detected is described hereinabove with reference to Figs. 2-8.

[3482] VGAM252 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Transmissible gastroenteritis virus. VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3483] VGAM252 gene, herein designated VGAM GENE, encodes a

VGAM252 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM252 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM252 precursor RNA is designated SEQ ID:6578, and is provided hereinbelow with reference to the sequence listing part.

[3484] VGAM252 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3485] An enzyme complex designated DICER COMPLEX, dices the VGAM252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM252 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM252 RNA is designated SEQ ID:6579, and is provided hereinbelow with reference to the sequence listing part.

[3486] VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3487] VGAM252 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM252 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM252 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3488] The complementary binding of VGAM252 RNA, herein designated VGAM RNA, to host target binding sites on VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM252 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[3489] It is appreciated that VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM252 host target genes. The mRNA of each one of this plurality of VGAM252 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM252 RNA, herein designated VGAM RNA, and which when bound by VGAM252 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM252 host target proteins.

[3490] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM252 gene, herein designated VGAM GENE, on one or more VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3491] It is yet further appreciated that a function of VGAM252 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM252 include diagnosis, prevention and treatment of viral infection by Transmissible gastroenteritis virus. Specific functions, and accordingly utilities, of VGAM252 correlate with, and may be deduced from, the identity of the host target genes which VGAM252 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3492] Nucleotide sequences of the VGAM252 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM252 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM252 are further described hereinbelow with reference to Table 1.

[3493] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM252 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3494] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 253 (VGAM253) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3495] VGAM253 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM253 was detected is described hereinabove with reference to Figs. 2-8.

[3496] VGAM253 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Transmissible gastroenteritis virus. VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3497] VGAM253 gene, herein designated VGAM GENE, encodes a VGAM253 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM253 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM253 precursor RNA is designated SEQ ID:6588, and is provided hereinbelow with reference to the sequence listing part.

[3498] VGAM253 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3499] An enzyme complex designated DICER COMPLEX, dices the VGAM253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM253 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM253 RNA is designated SEQ ID:6589, and is provided hereinbelow with reference to the sequence listing part.

[3500] VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3501] VGAM253 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM253 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3502] The complementary binding of VGAM253 RNA, herein designated VGAM RNA, to host target binding sites on VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM253 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3503] It is appreciated that VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM253 host target genes. The mRNA of each one of this plurality of VGAM253 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM253 RNA, herein designated VGAM RNA, and which when bound by VGAM253 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM253 host target proteins.

[3504] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM253 gene, herein designated VGAM GENE, on one or more VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3505] It is yet further appreciated that a function of VGAM253 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of viral infection by Transmissible gastroenteritis virus. Specific functions, and accordingly utilities, of VGAM253 correlate with, and may be deduced from, the identity of the host target genes which VGAM253 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3506] Nucleotide sequences of the VGAM253 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM253 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM253 are further described hereinbelow with reference to Table 1.

[3507] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM253 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3508] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 254 (VGAM254) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3509] VGAM254 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM254 was detected is described hereinabove with reference to Figs. 2–8.

[3510] VGAM254 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM254 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3511] VGAM254 gene, herein designated VGAM GENE, encodes a VGAM254 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM254 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM254 precursor RNA is designated SEQ ID:6600, and is provided hereinbelow with reference to the sequence listing part.

[3512] VGAM254 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3513] An enzyme complex designated DICER COMPLEX, dices the VGAM254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM254 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM254 RNA is designated SEQ ID:6601, and is provided hereinbelow with reference to the sequence listing part.

[3514] VGAM254 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3515] VGAM254 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM254 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM254 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3516] The complementary binding of VGAM254 RNA, herein designated VGAM RNA, to host target binding sites on VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM254 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3517] It is appreciated that VGAM254 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM254 host target genes. The mRNA of each one of this plurality of VGAM254 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM254 RNA, herein designated VGAM RNA, and which when bound by VGAM254 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM254 host target proteins.

[3518] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM254 gene, herein designated VGAM GENE, on one or more VGAM254 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3519] It is yet further appreciated that a function of VGAM254 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM254 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM254 correlate with, and may be deduced from, the identity of the host target genes which VGAM254 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3520] Nucleotide sequences of the VGAM254 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM254 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM254 are further described hereinbelow with reference to Table 1.

[3521] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM254 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3522] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 255 (VGAM255) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3523] VGAM255 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM255 was detected is described hereinabove with reference to Figs. 2–8.

[3524] VGAM255 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM255 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3525] VGAM255 gene, herein designated VGAM GENE, encodes a VGAM255 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM255 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM255 precursor RNA is designated SEQ ID:6611, and is provided hereinbelow with reference to the sequence listing part.

[3526] VGAM255 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3527] An enzyme complex designated DICER COMPLEX, dices the VGAM255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM255 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM255 RNA is designated SEQ ID:6612, and is provided hereinbelow with reference to the sequence listing part.

[3528] VGAM255 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3529] VGAM255 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM255 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM255 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3530] The complementary binding of VGAM255 RNA, herein designated VGAM RNA, to host target binding sites on VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM255 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3531] It is appreciated that VGAM255 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM255 host target genes. The mRNA of each one of this plurality of VGAM255 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM255 RNA, herein designated VGAM RNA, and which when bound by VGAM255 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM255 host target proteins.

[3532] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM255 gene, herein designated VGAM GENE, on one or more VGAM255 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[3533] It is yet further appreciated that a function of VGAM255 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM255 correlate with, and may be deduced from, the identity of the host target genes which VGAM255 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3534] Nucleotide sequences of the VGAM255 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM255 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM255 are further described hereinbelow with reference to Table 1.

[3535] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM255 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3536] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 256 (VGAM256) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3537] VGAM256 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM256 was detected is described hereinabove with reference to Figs. 2–8.

[3538] VGAM256 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM256 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3539] VGAM256 gene, herein designated VGAM GENE, encodes a VGAM256 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM256 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM256 precursor RNA is designated SEQ ID:6630, and is provided hereinbelow with reference to the sequence listing part.

[3540] VGAM256 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM256 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3541] An enzyme complex designated DICER COMPLEX, dices the VGAM256 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM256 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM256 RNA is designated SEQ ID:6631, and is provided hereinbelow with reference to the sequence listing part.

[3542] VGAM256 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3543] VGAM256 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM256 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3544] The complementary binding of VGAM256 RNA, herein designated VGAM RNA, to host target binding sites on VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM256 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3545] It is appreciated that VGAM256 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM256 host target genes. The mRNA of

each one of this plurality of VGAM256 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM256 RNA, herein designated VGAM RNA, and which when bound by VGAM256 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM256 host target proteins.

[3546] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM256 gene, herein designated VGAM GENE, on one or more VGAM256 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[3547] It is yet further appreciated that a function of VGAM256 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM256 correlate with, and may be deduced from, the identity of the host target genes which VGAM256 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3548] Nucleotide sequences of the VGAM256 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM256 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM256 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM256 are further described hereinbelow with reference to Table 1.

[3549] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM256 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[3550] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 257 (VGAM257) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3551] VGAM257 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM257 was detected is described hereinabove with reference to Figs. 2–8.

[3552] VGAM257 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine adenovirus D. VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3553] VGAM257 gene, herein designated VGAM GENE, encodes a VGAM257 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM257 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM257 precursor RNA is designated SEQ ID:6828, and is provided hereinbelow with reference to the sequence listing part.

[3554] VGAM257 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3555] An enzyme complex designated DICER COMPLEX, dices the VGAM257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM257 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM257 RNA is designated SEQ ID:6829, and



is provided hereinbelow with reference to the sequence listing part.

[3556] VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3557] VGAM257 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM257 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM257 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3558] The complementary binding of VGAM257 RNA, herein designated VGAM RNA, to host target binding sites on VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM257 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3559] It is appreciated that VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM257 host target genes. The mRNA of each one of this plurality of VGAM257 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM257 RNA, herein designated VGAM RNA, and which when bound by VGAM257 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM257 host target proteins.

[3560] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM257 gene, herein designated VGAM GENE, on one or more VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3561] It is yet further appreciated that a function of VGAM257 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of viral infection by Bovine adenovirus D. Specific functions, and accordingly utilities, of VGAM257 correlate with, and may be deduced from, the identity of the host target genes which VGAM257 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3562] Nucleotide sequences of the VGAM257 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM257 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM257 are further described hereinbelow with reference to Table 1.

[3563] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM257 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3564] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 258 (VGAM258) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3565] VGAM258 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM258 was detected is described hereinabove with reference to Figs. 2–8.

[3566] VGAM258 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3567] VGAM258 gene, herein designated VGAM GENE, encodes a VGAM258 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM258 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM258 precursor RNA is

designated SEQ ID:6840, and is provided hereinbelow with reference to the sequence listing part.

[3568] VGAM258 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3569] An enzyme complex designated DICER COMPLEX, dices the VGAM258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM258 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM258 RNA is designated SEQ ID:6841, and is provided hereinbelow with reference to the sequence

listing part.

[3570] VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3571] VGAM258 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM258 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3572] The complementary binding of VGAM258 RNA, herein designated VGAM RNA, to host target binding sites on VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM258 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3573] It is appreciated that VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM258 host target genes. The mRNA of each one of this plurality of VGAM258 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM258 RNA, herein designated VGAM RNA, and which when bound by VGAM258 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM258 host target proteins.

[3574] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM258 gene, herein designated VGAM GENE, on one or more VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3575] It is yet further appreciated that a function of VGAM258 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM258 correlate with, and may be deduced from, the identity of the host target genes which VGAM258 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3576] Nucleotide sequences of the VGAM258 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM258 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM258 are further described hereinbelow with reference to Table 1.

[3577] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM258 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3578] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 259 (VGAM259) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3579] VGAM259 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM259 was detected is described hereinabove with reference to Figs. 2–8.

[3580] VGAM259 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine adenovirus D. VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3581] VGAM259 gene, herein designated VGAM GENE, encodes a VGAM259 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM259 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM259 precursor RNA is designated SEQ ID:6846, and is provided hereinbelow with

reference to the sequence listing part.

[3582] VGAM259 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3583] An enzyme complex designated DICER COMPLEX, dices the VGAM259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM259 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM259 RNA is designated SEQ ID:6847, and is provided hereinbelow with reference to the sequence listing part.

[3584] VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3585] VGAM259 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM259 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3586] The complementary binding of VGAM259 RNA, herein designated VGAM RNA, to host target binding sites on VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM259 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3587] It is appreciated that VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM259 host target genes. The mRNA of each one of this plurality of VGAM259 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM259 RNA, herein designated VGAM RNA, and which when bound by VGAM259 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM259 host target proteins.

[3588] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM259 gene, herein designated VGAM GENE, on one or more VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3589] It is yet further appreciated that a function of VGAM259 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of viral infection by Bovine adenovirus D. Specific functions, and accordingly utilities, of VGAM259 correlate with, and may be deduced from, the identity of the host target genes which VGAM259 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3590] Nucleotide sequences of the VGAM259 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM259 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM259 are further described hereinbelow with reference to Table 1.

[3591] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM259 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3592] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 260 (VGAM260) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3593] VGAM260 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM260 was detected is described hereinabove with reference to Figs. 2–8.

[3594] VGAM260 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian hemorrhagic fever virus. VGAM260 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3595] VGAM260 gene, herein designated VGAM GENE, encodes a VGAM260 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM260 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM260 precursor RNA is designated SEQ ID:6857, and is provided hereinbelow with reference to the sequence listing part.

[3596] VGAM260 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3597] An enzyme complex designated DICER COMPLEX, dices the VGAM260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM260 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM260 RNA is designated SEQ ID:6858, and is provided hereinbelow with reference to the sequence listing part.

[3598] VGAM260 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3599] VGAM260 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM260 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3600] The complementary binding of VGAM260 RNA, herein designated VGAM RNA, to host target binding sites on VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM260 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3601] It is appreciated that VGAM260 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM260 host target genes. The mRNA of each one of this plurality of VGAM260 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM260 RNA, herein designated VGAM

RNA, and which when bound by VGAM260 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM260 host target proteins.

[3602] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM260 gene, herein designated VGAM GENE, on one or more VGAM260 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3603] It is yet further appreciated that a function of VGAM260 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM260 include diagnosis, prevention and treatment of viral infection by Simian hemorrhagic fever virus. Specific functions, and accordingly utilities, of VGAM260 correlate with, and may be deduced from, the identity of the host target genes which VGAM260 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3604] Nucleotide sequences of the VGAM260 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM260 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM260 are further described hereinbelow with reference to Table 1.

[3605] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM260 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3606] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 261 (VGAM261) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3607] VGAM261 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM261 was detected is described hereinabove with reference to Figs. 2–8.

[3608] VGAM261 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3609] VGAM261 gene, herein designated VGAM GENE, encodes a VGAM261 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM261 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM261 precursor RNA is designated SEQ ID:6863, and is provided hereinbelow with reference to the sequence listing part.

[3610] VGAM261 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3611] An enzyme complex designated DICER COMPLEX, dices the VGAM261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM261 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM261 RNA is designated SEQ ID:6864, and is provided hereinbelow with reference to the sequence listing part.

[3612] VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3613] VGAM261 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM261 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM261 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3614] The complementary binding of VGAM261 RNA, herein designated VGAM RNA, to host target binding sites on VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM261 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3615] It is appreciated that VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM261 host target genes. The mRNA of each one of this plurality of VGAM261 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM261 RNA, herein designated VGAM RNA, and which when bound by VGAM261 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM261 host target proteins.

[3616] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM261 gene, herein designated VGAM GENE, on one or more VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3617] It is yet further appreciated that a function of VGAM261 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM261 include diagnosis, prevention and

treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM261 correlate with, and may be deduced from, the identity of the host target genes which VGAM261 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3618] Nucleotide sequences of the VGAM261 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM261 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM261 are further described hereinbelow with reference to Table 1.

[3619] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM261 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3620] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 262 (VGAM262) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3621] VGAM262 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM262 was detected is described hereinabove with reference to Figs. 2–8.

[3622] VGAM262 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3623] VGAM262 gene, herein designated VGAM GENE, encodes a VGAM262 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM262 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM262 precursor RNA is designated SEQ ID:6917, and is provided hereinbelow with reference to the sequence listing part.

[3624] VGAM262 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM262 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3625] An enzyme complex designated DICER COMPLEX, dices the VGAM262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM262 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM262 RNA is designated SEQ ID:6918, and is provided hereinbelow with reference to the sequence listing part.

[3626] VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM262 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3627] VGAM262 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM262 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM262 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3628] The complementary binding of VGAM262 RNA, herein designated VGAM RNA, to host target binding sites on VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM262 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3629] It is appreciated that VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM262 host target genes. The mRNA of each one of this plurality of VGAM262 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM262 RNA, herein designated VGAM RNA, and which when bound by VGAM262 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM262 host target proteins.

[3630] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM262 gene, herein designated VGAM GENE, on one or more VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3631] It is yet further appreciated that a function of VGAM262 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM262 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Spe-

cific functions, and accordingly utilities, of VGAM262 correlate with, and may be deduced from, the identity of the host target genes which VGAM262 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3632] Nucleotide sequences of the VGAM262 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM262 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM262 are further described hereinbelow with reference to Table 1.

[3633] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM262 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3634] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 263 (VGAM263) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[3635] VGAM263 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM263 was detected is described hereinabove with reference to Figs. 2–8.

[3636] VGAM263 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian hemorrhagic fever virus. VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3637] VGAM263 gene, herein designated VGAM GENE, encodes a VGAM263 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM263 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM263 precursor RNA is designated SEQ ID:6976, and is provided hereinbelow with reference to the sequence listing part.

[3638] VGAM263 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM263 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3639] An enzyme complex designated DICER COMPLEX, dices the VGAM263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM263 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM263 RNA is designated SEQ ID:6977, and is provided hereinbelow with reference to the sequence listing part.

[3640] VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM263 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3641] VGAM263 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM263 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM263 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3642] The complementary binding of VGAM263 RNA, herein designated VGAM RNA, to host target binding sites on VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM263 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3643] It is appreciated that VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM263 host target genes. The mRNA of each one of this plurality of VGAM263 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM263 RNA, herein designated VGAM RNA, and which when bound by VGAM263 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM263 host target proteins.

[3644] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM263 gene, herein designated VGAM GENE, on one or more VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3645] It is yet further appreciated that a function of VGAM263 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM263 include diagnosis, prevention and treatment of viral infection by Simian hemorrhagic fever virus. Specific functions, and accordingly utilities, of

VGAM263 correlate with, and may be deduced from, the identity of the host target genes which VGAM263 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3646] Nucleotide sequences of the VGAM263 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM263 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM263 are further described hereinbelow with reference to Table 1.

[3647] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM263 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3648] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 264 (VGAM264) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[3649] VGAM264 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM264 was detected is described hereinabove with reference to Figs. 2–8.

[3650] VGAM264 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian hemorrhagic fever virus. VGAM264 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3651] VGAM264 gene, herein designated VGAM GENE, encodes a VGAM264 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM264 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM264 precursor RNA is designated SEQ ID:6980, and is provided hereinbelow with reference to the sequence listing part.

[3652] VGAM264 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3653] An enzyme complex designated DICER COMPLEX, dices the VGAM264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM264 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM264 RNA is designated SEQ ID:6981, and is provided hereinbelow with reference to the sequence listing part.

[3654] VGAM264 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3655] VGAM264 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM264 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3656] The complementary binding of VGAM264 RNA, herein designated VGAM RNA, to host target binding sites on VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM264 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3657] It is appreciated that VGAM264 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM264 host target genes. The mRNA of each one of this plurality of VGAM264 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM264 RNA, herein designated VGAM RNA, and which when bound by VGAM264 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM264 host target proteins.

[3658] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM264 gene, herein designated VGAM GENE, on one or more VGAM264 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3659] It is yet further appreciated that a function of VGAM264 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of viral infection by Simian hemorrhagic fever virus. Specific functions, and accordingly utilities, of VGAM264 correlate with, and may be deduced from, the

identity of the host target genes which VGAM264 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3660] Nucleotide sequences of the VGAM264 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM264 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM264 are further described hereinbelow with reference to Table 1.

[3661] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM264 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3662] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 265 (VGAM265) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3663] VGAM265 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM265 was detected is described hereinabove with reference to Figs. 2–8.

[3664] VGAM265 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM265 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3665] VGAM265 gene, herein designated VGAM GENE, encodes a VGAM265 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM265 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM265 precursor RNA is designated SEQ ID:6995, and is provided hereinbelow with reference to the sequence listing part.

[3666] VGAM265 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3667] An enzyme complex designated DICER COMPLEX, dices the VGAM265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM265 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM265 RNA is designated SEQ ID:6996, and is provided hereinbelow with reference to the sequence listing part.

[3668] VGAM265 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5



untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3669] VGAM265 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM265 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3670] The complementary binding of VGAM265 RNA, herein designated VGAM RNA, to host target binding sites on VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM265 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3671] It is appreciated that VGAM265 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM265 host target genes. The mRNA of each one of this plurality of VGAM265 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM265 RNA, herein designated VGAM RNA, and which when bound by VGAM265 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM265 host target proteins.

[3672] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM265 gene, herein designated VGAM GENE, on one or more VGAM265 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3673] It is yet further appreciated that a function of VGAM265 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM265 correlate with, and may be deduced from, the identity of the host target genes which VGAM265 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[3674] Nucleotide sequences of the VGAM265 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM265 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM265 are further described hereinbelow with reference to Table 1.

[3675] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM265 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3676] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 266 (VGAM266) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3677] VGAM266 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM266 was detected is described hereinabove with reference to Figs. 2–8.

[3678] VGAM266 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian hemorrhagic fever virus. VGAM266 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3679] VGAM266 gene, herein designated VGAM GENE, encodes a VGAM266 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM266 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM266 precursor RNA is designated SEQ ID:7054, and is provided hereinbelow with reference to the sequence listing part.

[3680] VGAM266 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3681] An enzyme complex designated DICER COMPLEX, dices the VGAM266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM266 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM266 RNA is designated SEQ ID:7055, and is provided hereinbelow with reference to the sequence listing part.

[3682] VGAM266 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3683] VGAM266 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM266 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[3684] The complementary binding of VGAM266 RNA, herein designated VGAM RNA, to host target binding sites on VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM266 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3685] It is appreciated that VGAM266 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM266 host target genes. The mRNA of each one of this plurality of VGAM266 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM266 RNA, herein designated VGAM RNA, and which when bound by VGAM266 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM266 host target proteins.

[3686] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM266 gene, herein designated VGAM GENE, on one or more VGAM266 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3687] It is yet further appreciated that a function of VGAM266 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of viral infection by Simian hemorrhagic fever virus. Specific functions, and accordingly utilities, of VGAM266 correlate with, and may be deduced from, the identity of the host target genes which VGAM266 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[3688] Nucleotide sequences of the VGAM266 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM266 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM266 are further described hereinbelow with reference to Table 1.

[3689] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM266 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3690] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 267 (VGAM267) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3691] VGAM267 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM267 was detected is described hereinabove with reference to Figs. 2–8.

[3692] VGAM267 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3693] VGAM267 gene, herein designated VGAM GENE, encodes a VGAM267 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM267 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM267 precursor RNA is designated SEQ ID:7064, and is provided hereinbelow with reference to the sequence listing part.

[3694] VGAM267 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3695] An enzyme complex designated DICER COMPLEX, dices the VGAM267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM267 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM267 RNA is designated SEQ ID:7065, and is provided hereinbelow with reference to the sequence listing part.

[3696] VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[3697] VGAM267 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM267 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM267 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3698] The complementary binding of VGAM267 RNA, herein designated VGAM RNA, to host target binding sites on VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM267 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3699] It is appreciated that VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM267 host target genes. The mRNA of each one of this plurality of VGAM267 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM267 RNA, herein designated VGAM RNA, and which when bound by VGAM267 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM267 host target proteins.

[3700] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM267 gene, herein designated VGAM GENE, on one or

more VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3701] It is yet further appreciated that a function of VGAM267 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM267 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM267 correlate with, and may be deduced from, the identity of the host target genes which VGAM267 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3702] Nucleotide sequences of the VGAM267 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM267 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM267 are further described hereinbelow with reference to Table 1.

[3703] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM267 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3704] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 268 (VGAM268) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3705] VGAM268 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM268 was detected is described



hereinabove with reference to Figs. 2–8.

[3706] VGAM268 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM268 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3707] VGAM268 gene, herein designated VGAM GENE, encodes a VGAM268 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM268 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM268 precursor RNA is designated SEQ ID:7127, and is provided hereinbelow with reference to the sequence listing part.

[3708] VGAM268 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3709] An enzyme complex designated DICER COMPLEX, dices the VGAM268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM268 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM268 RNA is designated SEQ ID:7128, and is provided hereinbelow with reference to the sequence listing part.

[3710] VGAM268 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3711] VGAM268 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM268 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM268 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3712] The complementary binding of VGAM268 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM268 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3713] It is appreciated that VGAM268 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM268 host target genes. The mRNA of each one of this plurality of VGAM268 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM268 RNA, herein designated VGAM RNA, and which when bound by VGAM268 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM268 host target proteins.

[3714] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM268 gene, herein designated VGAM GENE, on one or more VGAM268 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3715] It is yet further appreciated that a function of VGAM268 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM268 correlate with, and may be deduced from, the identity of the host target genes which VGAM268 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3716] Nucleotide sequences of the VGAM268 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM268 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM268 are further described hereinbelow with reference to Table 1.

[3717] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM268 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3718] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 269 (VGAM269) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3719] VGAM269 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM269 was detected is described hereinabove with reference to Figs. 2-8.

[3720] VGAM269 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3721] VGAM269 gene, herein designated VGAM GENE, encodes a VGAM269 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM269 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM269 precursor RNA is designated SEQ ID:7142, and is provided hereinbelow with reference to the sequence listing part.

[3722] VGAM269 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[3723] An enzyme complex designated DICER COMPLEX, dices the VGAM269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM269 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM269 RNA is designated SEQ ID:7143, and is provided hereinbelow with reference to the sequence listing part.

[3724] VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3725] VGAM269 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM269 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM269 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3726] The complementary binding of VGAM269 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM269 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3727] It is appreciated that VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM269 host target genes. The mRNA of each one of this plurality of VGAM269 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM269 RNA, herein designated VGAM RNA, and which when bound by VGAM269 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM269 host target proteins.

[3728] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM269 gene, herein designated VGAM GENE, on one or more VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3729] It is yet further appreciated that a function of VGAM269 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM269 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM269 correlate with, and may be deduced from, the identity of the host target genes which VGAM269 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3730] Nucleotide sequences of the VGAM269 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM269 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM269 are further described hereinbelow with reference to Table 1.

[3731] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM269 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3732] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 270 (VGAM270) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3733] VGAM270 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM270 was detected is described hereinabove with reference to Figs. 2-8.

[3734] VGAM270 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine herpesvirus 2. VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3735] VGAM270 gene, herein designated VGAM GENE, encodes a VGAM270 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM270 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM270 precursor RNA is designated SEQ ID:7152, and is provided hereinbelow with reference to the sequence listing part.

[3736] VGAM270 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3737] An enzyme complex designated DICER COMPLEX, dices the VGAM270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM270 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM270 RNA is designated SEQ ID:7153, and is provided hereinbelow with reference to the sequence listing part.

[3738] VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3739] VGAM270 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM270 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3740] The complementary binding of VGAM270 RNA, herein designated VGAM RNA, to host target binding sites on VGAM270 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM270 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3741] It is appreciated that VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM270 host target genes. The mRNA of each one of this plurality of VGAM270 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM270 RNA, herein designated VGAM RNA, and which when bound by VGAM270 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM270 host target proteins.

[3742] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM270 gene, herein designated VGAM GENE, on one or more VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3743] It is yet further appreciated that a function of VGAM270 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM270 correlate with, and may be deduced from, the identity of the host target genes which VGAM270 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3744] Nucleotide sequences of the VGAM270 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM270 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM270 are further described hereinbelow with reference to Table 1.

[3745] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM270 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3746] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 271 (VGAM271) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3747] VGAM271 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM271 was detected is described hereinabove with reference to Figs. 2-8.

[3748] VGAM271 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2.

VGAM271 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3749] VGAM271 gene, herein designated VGAM GENE, encodes a VGAM271 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM271 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM271 precursor RNA is designated SEQ ID:7166, and is provided hereinbelow with reference to the sequence listing part.

[3750] VGAM271 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3751] An enzyme complex designated DICER COMPLEX, dices

the VGAM271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM271 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM271 RNA is designated SEQ ID:7167, and is provided hereinbelow with reference to the sequence listing part.

[3752] VGAM271 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3753] VGAM271 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM271 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM271 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3754] The complementary binding of VGAM271 RNA, herein designated VGAM RNA, to host target binding sites on VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM271 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3755] It is appreciated that VGAM271 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM271 host target genes. The mRNA of each one of this plurality of VGAM271 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM271 RNA, herein designated VGAM RNA, and which when bound by VGAM271 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM271 host target proteins.

[3756] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM271 gene, herein designated VGAM GENE, on one or more VGAM271 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3757] It is yet further appreciated that a function of VGAM271 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM271 correlate with, and may be deduced from, the identity of the host target genes which VGAM271 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3758] Nucleotide sequences of the VGAM271 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM271 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM271 are further described hereinbelow with reference to Table 1.

[3759] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM271 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3760] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 272 (VGAM272) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3761] VGAM272 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM272 was detected is described hereinabove with reference to Figs. 2-8.

[3762] VGAM272 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM272 host target gene, herein designated VGAM HOST TARGET



GENE, is a human gene contained in the human genome.

[3763] VGAM272 gene, herein designated VGAM GENE, encodes a VGAM272 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM272 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM272 precursor RNA is designated SEQ ID:7181, and is provided hereinbelow with reference to the sequence listing part.

[3764] VGAM272 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3765] An enzyme complex designated DICER COMPLEX, dices the VGAM272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM272 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM272 RNA is designated SEQ ID:7182, and is provided hereinbelow with reference to the sequence listing part.

[3766] VGAM272 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3767] VGAM272 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM272 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM272 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3768] The complementary binding of VGAM272 RNA, herein designated VGAM RNA, to host target binding sites on VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM272 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3769] It is appreciated that VGAM272 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM272 host target genes. The mRNA of each one of this plurality of VGAM272 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM272 RNA, herein designated VGAM RNA, and which when bound by VGAM272 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM272 host target proteins.

[3770] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM272 gene, herein designated VGAM GENE, on one or more VGAM272 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3771] It is yet further appreciated that a function of VGAM272 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM272 correlate with, and may be deduced from, the identity of the host target genes which VGAM272 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3772] Nucleotide sequences of the VGAM272 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM272 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM272 are further de-

scribed hereinbelow with reference to Table 1.

[3773] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM272 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3774] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 273 (VGAM273) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3775] VGAM273 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM273 was detected is described hereinabove with reference to Figs. 2-8.

[3776] VGAM273 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3777] VGAM273 gene, herein designated VGAM GENE, encodes a

VGAM273 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM273 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM273 precursor RNA is designated SEQ ID:7194, and is provided hereinbelow with reference to the sequence listing part.

[3778] VGAM273 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3779] An enzyme complex designated DICER COMPLEX, dices the VGAM273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM273 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM273 RNA is designated SEQ ID:7195, and is provided hereinbelow with reference to the sequence listing part.

[3780] VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3781] VGAM273 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed



sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM273 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3782] The complementary binding of VGAM273 RNA, herein designated VGAM RNA, to host target binding sites on VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM273 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[3783] It is appreciated that VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM273 host target genes. The mRNA of each one of this plurality of VGAM273 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM273 RNA, herein designated VGAM RNA, and which when bound by VGAM273 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM273 host target proteins.

[3784] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM273 gene, herein designated VGAM GENE, on one or more VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3785] It is yet further appreciated that a function of VGAM273 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM273 correlate with, and may be deduced from, the identity of the host target genes which VGAM273 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3786] Nucleotide sequences of the VGAM273 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM273 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM273 are further described hereinbelow with reference to Table 1.

[3787] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM273 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3788] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 274 (VGAM274) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3789] VGAM274 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM274 was detected is described hereinabove with reference to Figs. 2-8.

[3790] VGAM274 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3791] VGAM274 gene, herein designated VGAM GENE, encodes a VGAM274 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM274 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM274 precursor RNA is designated SEQ ID:7198, and is provided hereinbelow with reference to the sequence listing part.

[3792] VGAM274 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3793] An enzyme complex designated DICER COMPLEX, dices the VGAM274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM274 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM274 RNA is designated SEQ ID:7199, and is provided hereinbelow with reference to the sequence listing part.

[3794] VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3795] VGAM274 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM274 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM274 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3796] The complementary binding of VGAM274 RNA, herein designated VGAM RNA, to host target binding sites on VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM274 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3797] It is appreciated that VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM274 host target genes. The mRNA of each one of this plurality of VGAM274 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM274 RNA, herein designated VGAM RNA, and which when bound by VGAM274 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM274 host target proteins.

[3798] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM274 gene, herein designated VGAM GENE, on one or more VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-



though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3799] It is yet further appreciated that a function of VGAM274 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM274 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM274 correlate with, and may be deduced from, the identity of the host target genes which VGAM274 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3800] Nucleotide sequences of the VGAM274 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM274 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM274 are further described hereinbelow with reference to Table 1.

[3801] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM274 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3802] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 275 (VGAM275) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3803] VGAM275 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM275 was detected is described hereinabove with reference to Figs. 2–8.

[3804] VGAM275 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM275 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3805] VGAM275 gene, herein designated VGAM GENE, encodes a VGAM275 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM275 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM275 precursor RNA is designated SEQ ID:7219, and is provided hereinbelow with reference to the sequence listing part.

[3806] VGAM275 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3807] An enzyme complex designated DICER COMPLEX, dices the VGAM275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM275 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM275 RNA is designated SEQ ID:7220, and is provided hereinbelow with reference to the sequence listing part.

[3808] VGAM275 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3809] VGAM275 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM275 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM275 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3810] The complementary binding of VGAM275 RNA, herein designated VGAM RNA, to host target binding sites on VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM275 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3811] It is appreciated that VGAM275 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM275 host target genes. The mRNA of each one of this plurality of VGAM275 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM275 RNA, herein designated VGAM RNA, and which when bound by VGAM275 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM275 host target proteins.

[3812] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM275 gene, herein designated VGAM GENE, on one or more VGAM275 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3813] It is yet further appreciated that a function of VGAM275 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM275 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM275 correlate with, and may be deduced from, the identity of the host target genes which VGAM275 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3814] Nucleotide sequences of the VGAM275 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM275 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM275 are further described hereinbelow with reference to Table 1.

[3815] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM275 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3816] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 276 (VGAM276) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3817] VGAM276 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM276 was detected is described hereinabove with reference to Figs. 2–8.

[3818] VGAM276 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3819] VGAM276 gene, herein designated VGAM GENE, encodes a VGAM276 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM276 precursor RNA, herein



designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM276 precursor RNA is designated SEQ ID:7229, and is provided hereinbelow with reference to the sequence listing part.

[3820] VGAM276 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3821] An enzyme complex designated DICER COMPLEX, dices the VGAM276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM276 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM276 RNA is designated SEQ ID:7230, and is provided hereinbelow with reference to the sequence listing part.

[3822] VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3823] VGAM276 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM276 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3824] The complementary binding of VGAM276 RNA, herein designated VGAM RNA, to host target binding sites on VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM276 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3825] It is appreciated that VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM276 host target genes. The mRNA of each one of this plurality of VGAM276 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM276 RNA, herein designated VGAM RNA, and which when bound by VGAM276 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM276 host target proteins.

[3826] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM276 gene, herein designated VGAM GENE, on one or more VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[3827] It is yet further appreciated that a function of VGAM276 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM276 correlate with, and may be deduced from, the identity of the host target genes which VGAM276 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3828] Nucleotide sequences of the VGAM276 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM276 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM276 are further described hereinbelow with reference to Table 1.

[3829] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM276 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3830] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 277 (VGAM277) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3831] VGAM277 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM277 was detected is described hereinabove with reference to Figs. 2-8.

[3832] VGAM277 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3833] VGAM277 gene, herein designated VGAM GENE, encodes a VGAM277 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM277 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM277 precursor RNA is designated SEQ ID:7247, and is provided hereinbelow with reference to the sequence listing part.

[3834] VGAM277 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3835] An enzyme complex designated DICER COMPLEX, dices the VGAM277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM277 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM277 RNA is designated SEQ ID:7248, and

is provided hereinbelow with reference to the sequence listing part.

[3836] VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3837] VGAM277 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM277 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3838] The complementary binding of VGAM277 RNA, herein designated VGAM RNA, to host target binding sites on VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM277 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3839] It is appreciated that VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM277 host target genes. The mRNA of each one of this plurality of VGAM277 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM277 RNA, herein designated VGAM RNA, and which when bound by VGAM277 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM277 host target proteins.

[3840] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM277 gene, herein designated VGAM GENE, on one or more VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3841] It is yet further appreciated that a function of VGAM277 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM277 correlate with, and may be deduced from, the identity of the host target genes which VGAM277 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3842] Nucleotide sequences of the VGAM277 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM277 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM277 are further described hereinbelow with reference to Table 1.

[3843] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM277 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3844] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 278 (VGAM278) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3845] VGAM278 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM278 was detected is described hereinabove with reference to Figs. 2–8.

[3846] VGAM278 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3847] VGAM278 gene, herein designated VGAM GENE, encodes a VGAM278 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM278 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM278 precursor RNA is

designated SEQ ID:7265, and is provided hereinbelow with reference to the sequence listing part.

[3848] VGAM278 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3849] An enzyme complex designated DICER COMPLEX, dices the VGAM278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM278 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM278 RNA is designated SEQ ID:7266, and is provided hereinbelow with reference to the sequence

listing part.

[3850] VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3851] VGAM278 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM278 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM278 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3852] The complementary binding of VGAM278 RNA, herein designated VGAM RNA, to host target binding sites on VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM278 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3853] It is appreciated that VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM278 host target genes. The mRNA of each one of this plurality of VGAM278 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM278 RNA, herein designated VGAM RNA, and which when bound by VGAM278 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM278 host target proteins.

[3854] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM278 gene, herein designated VGAM GENE, on one or more VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3855] It is yet further appreciated that a function of VGAM278 is



inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM278 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM278 correlate with, and may be deduced from, the identity of the host target genes which VGAM278 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3856] Nucleotide sequences of the VGAM278 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM278 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM278 are further described hereinbelow with reference to Table 1.

[3857] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM278 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3858] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 279 (VGAM279) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3859] VGAM279 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM279 was detected is described hereinabove with reference to Figs. 2–8.

[3860] VGAM279 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3861] VGAM279 gene, herein designated VGAM GENE, encodes a VGAM279 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM279 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM279 precursor RNA is designated SEQ ID:7274, and is provided hereinbelow with

reference to the sequence listing part.

[3862] VGAM279 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3863] An enzyme complex designated DICER COMPLEX, dices the VGAM279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM279 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM279 RNA is designated SEQ ID:7275, and is provided hereinbelow with reference to the sequence listing part.

[3864] VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3865] VGAM279 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM279 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3866] The complementary binding of VGAM279 RNA, herein designated VGAM RNA, to host target binding sites on VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM279 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3867] It is appreciated that VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM279 host target genes. The mRNA of each one of this plurality of VGAM279 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM279 RNA, herein designated VGAM RNA, and which when bound by VGAM279 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM279 host target proteins.

[3868] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM279 gene, herein designated VGAM GENE, on one or more VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3869] It is yet further appreciated that a function of VGAM279 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM279 correlate with, and may be deduced from, the identity of the host target genes which VGAM279 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3870] Nucleotide sequences of the VGAM279 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM279 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM279 are further described hereinbelow with reference to Table 1.

[3871] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM279 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3872] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 280 (VGAM280) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3873] VGAM280 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM280 was detected is described hereinabove with reference to Figs. 2–8.

[3874] VGAM280 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM280 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3875] VGAM280 gene, herein designated VGAM GENE, encodes a VGAM280 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM280 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM280 precursor RNA is designated SEQ ID:7280, and is provided hereinbelow with reference to the sequence listing part.



[3876] VGAM280 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3877] An enzyme complex designated DICER COMPLEX, dices the VGAM280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM280 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM280 RNA is designated SEQ ID:7281, and is provided hereinbelow with reference to the sequence listing part.

[3878] VGAM280 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3879] VGAM280 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM280 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3880] The complementary binding of VGAM280 RNA, herein designated VGAM RNA, to host target binding sites on VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM280 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3881] It is appreciated that VGAM280 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM280 host target genes. The mRNA of each one of this plurality of VGAM280 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM280 RNA, herein designated VGAM

RNA, and which when bound by VGAM280 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM280 host target proteins.

[3882] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM280 gene, herein designated VGAM GENE, on one or more VGAM280 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3883] It is yet further appreciated that a function of VGAM280 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM280 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM280 correlate with, and may be deduced from, the identity of the host target genes which VGAM280 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3884] Nucleotide sequences of the VGAM280 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM280 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM280 are further described hereinbelow with reference to Table 1.

[3885] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM280 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3886] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 281 (VGAM281) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3887] VGAM281 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM281 was detected is described hereinabove with reference to Figs. 2–8.

[3888] VGAM281 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3889] VGAM281 gene, herein designated VGAM GENE, encodes a VGAM281 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM281 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM281 precursor RNA is designated SEQ ID:7297, and is provided hereinbelow with reference to the sequence listing part.

[3890] VGAM281 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM281 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3891] An enzyme complex designated DICER COMPLEX, dices the VGAM281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM281 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM281 RNA is designated SEQ ID:7182, and is provided hereinbelow with reference to the sequence listing part.

[3892] VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM281 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3893] VGAM281 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM281 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3894] The complementary binding of VGAM281 RNA, herein designated VGAM RNA, to host target binding sites on VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM281 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3895] It is appreciated that VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM281 host target genes. The mRNA of each one of this plurality of VGAM281 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM281 RNA, herein designated VGAM RNA, and which when bound by VGAM281 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM281 host target proteins.

[3896] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM281 gene, herein designated VGAM GENE, on one or more VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3897] It is yet further appreciated that a function of VGAM281 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific

functions, and accordingly utilities, of VGAM281 correlate with, and may be deduced from, the identity of the host target genes which VGAM281 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3898] Nucleotide sequences of the VGAM281 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM281 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM281 are further described hereinbelow with reference to Table 1.

[3899] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM281 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3900] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 282 (VGAM282) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[3901] VGAM282 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM282 was detected is described hereinabove with reference to Figs. 2–8.

[3902] VGAM282 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM282 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3903] VGAM282 gene, herein designated VGAM GENE, encodes a VGAM282 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM282 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM282 precursor RNA is designated SEQ ID:7298, and is provided hereinbelow with reference to the sequence listing part.

[3904] VGAM282 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM282 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3905] An enzyme complex designated DICER COMPLEX, dices the VGAM282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM282 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM282 RNA is designated SEQ ID:7299, and is provided hereinbelow with reference to the sequence listing part.

[3906] VGAM282 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM282 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3907] VGAM282 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM282 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM282 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3908] The complementary binding of VGAM282 RNA, herein designated VGAM RNA, to host target binding sites on VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM282 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3909] It is appreciated that VGAM282 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM282 host target genes. The mRNA of each one of this plurality of VGAM282 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM282 RNA, herein designated VGAM RNA, and which when bound by VGAM282 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM282 host target proteins.

[3910] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM282 gene, herein designated VGAM GENE, on one or more VGAM282 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3911] It is yet further appreciated that a function of VGAM282 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM282 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM282 cor-



relate with, and may be deduced from, the identity of the host target genes which VGAM282 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3912] Nucleotide sequences of the VGAM282 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM282 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM282 are further described hereinbelow with reference to Table 1.

[3913] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM282 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3914] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 283 (VGAM283) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[3915] VGAM283 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM283 was detected is described hereinabove with reference to Figs. 2–8.

[3916] VGAM283 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3917] VGAM283 gene, herein designated VGAM GENE, encodes a VGAM283 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM283 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM283 precursor RNA is designated SEQ ID:7313, and is provided hereinbelow with reference to the sequence listing part.

[3918] VGAM283 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3919] An enzyme complex designated DICER COMPLEX, dices the VGAM283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM283 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM283 RNA is designated SEQ ID:7314, and is provided hereinbelow with reference to the sequence listing part.

[3920] VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3921] VGAM283 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM283 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM283 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3922] The complementary binding of VGAM283 RNA, herein designated VGAM RNA, to host target binding sites on VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM283 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3923] It is appreciated that VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM283 host target genes. The mRNA of each one of this plurality of VGAM283 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM283 RNA, herein designated VGAM RNA, and which when bound by VGAM283 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM283 host target proteins.

[3924] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM283 gene, herein designated VGAM GENE, on one or more VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3925] It is yet further appreciated that a function of VGAM283 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM283 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM283 correlate with, and may be deduced from, the identity of the

host target genes which VGAM283 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3926] Nucleotide sequences of the VGAM283 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM283 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM283 are further described hereinbelow with reference to Table 1.

[3927] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM283 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3928] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 284 (VGAM284) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3929] VGAM284 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM284 was detected is described hereinabove with reference to Figs. 2–8.

[3930] VGAM284 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM284 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3931] VGAM284 gene, herein designated VGAM GENE, encodes a VGAM284 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM284 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM284 precursor RNA is designated SEQ ID:7333, and is provided hereinbelow with reference to the sequence listing part.

[3932] VGAM284 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the



fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3933] An enzyme complex designated DICER COMPLEX, dices the VGAM284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM284 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM284 RNA is designated SEQ ID:7334, and is provided hereinbelow with reference to the sequence listing part.

[3934] VGAM284 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3935] VGAM284 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM284 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM284 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3'UTR and 5'UTR regions.

[3936] The complementary binding of VGAM284 RNA, herein designated VGAM RNA, to host target binding sites on VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM284 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3937] It is appreciated that VGAM284 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM284 host target genes. The mRNA of each one of this plurality of VGAM284 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM284 RNA, herein designated VGAM RNA, and which when bound by VGAM284 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM284 host target proteins.

[3938] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM284 gene, herein designated VGAM GENE, on one or more VGAM284 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3939] It is yet further appreciated that a function of VGAM284 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM284 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM284 correlate with, and may be deduced from, the identity of the host target genes which VGAM284 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[3940] Nucleotide sequences of the VGAM284 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM284 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM284 are further described hereinbelow with reference to Table 1.

[3941] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM284 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3942] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 285 (VGAM285) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3943] VGAM285 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM285 was detected is described hereinabove with reference to Figs. 2–8.

[3944] VGAM285 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3945] VGAM285 gene, herein designated VGAM GENE, encodes a VGAM285 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM285 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM285 precursor RNA is designated SEQ ID:7342, and is provided hereinbelow with reference to the sequence listing part.

[3946] VGAM285 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3947] An enzyme complex designated DICER COMPLEX, dices the VGAM285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM285 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM285 RNA is designated SEQ ID:7343, and is provided hereinbelow with reference to the sequence listing part.

[3948] VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[3949] VGAM285 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM285 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM285 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[3950] The complementary binding of VGAM285 RNA, herein designated VGAM RNA, to host target binding sites on VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM285 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3951] It is appreciated that VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM285 host target genes. The mRNA of each one of this plurality of VGAM285 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM285 RNA, herein designated VGAM RNA, and which when bound by VGAM285 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM285 host target proteins.

[3952] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM285 gene, herein designated VGAM GENE, on one or

more VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3953] It is yet further appreciated that a function of VGAM285 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM285 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM285 correlate with, and may be deduced from, the identity of the host target genes which VGAM285 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3954] Nucleotide sequences of the VGAM285 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM285 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM285 are further described hereinbelow with reference to Table 1.

[3955] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM285 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3956] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 286 (VGAM286) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3957] VGAM286 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM286 was detected is described

hereinabove with reference to Figs. 2–8.

[3958] VGAM286 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM286 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3959] VGAM286 gene, herein designated VGAM GENE, encodes a VGAM286 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM286 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM286 precursor RNA is designated SEQ ID:7451, and is provided hereinbelow with reference to the sequence listing part.

[3960] VGAM286 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3961] An enzyme complex designated DICER COMPLEX, dices the VGAM286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM286 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM286 RNA is designated SEQ ID:7452, and is provided hereinbelow with reference to the sequence listing part.

[3962] VGAM286 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3963] VGAM286 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM286 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM286 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3964] The complementary binding of VGAM286 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM286 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3965] It is appreciated that VGAM286 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM286 host target genes. The mRNA of each one of this plurality of VGAM286 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM286 RNA, herein designated VGAM RNA, and which when bound by VGAM286 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM286 host target proteins.

[3966] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM286 gene, herein designated VGAM GENE, on one or more VGAM286 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3967] It is yet further appreciated that a function of VGAM286 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM286 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM286 correlate with, and may be deduced from, the identity of the host target genes which VGAM286 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3968] Nucleotide sequences of the VGAM286 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM286 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM286 are further described hereinbelow with reference to Table 1.

[3969] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM286 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3970] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 287 (VGAM287) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3971] VGAM287 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM287 was detected is described hereinabove with reference to Figs. 2-8.

[3972] VGAM287 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3973] VGAM287 gene, herein designated VGAM GENE, encodes a VGAM287 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM287 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM287 precursor RNA is designated SEQ ID:7466, and is provided hereinbelow with reference to the sequence listing part.

[3974] VGAM287 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3975] An enzyme complex designated DICER COMPLEX, dices the VGAM287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM287 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM287 RNA is designated SEQ ID:7467, and is provided hereinbelow with reference to the sequence listing part.

[3976] VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3977] VGAM287 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM287 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM287 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3978] The complementary binding of VGAM287 RNA, herein designated VGAM RNA, to host target binding sites on VGAM287 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM287 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3979] It is appreciated that VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM287 host target genes. The mRNA of each one of this plurality of VGAM287 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM287 RNA, herein designated VGAM RNA, and which when bound by VGAM287 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM287 host target proteins.

[3980] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM287 gene, herein designated VGAM GENE, on one or more VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3981] It is yet further appreciated that a function of VGAM287 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM287 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM287 correlate with, and may be deduced from, the identity of the host target genes which VGAM287 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3982] Nucleotide sequences of the VGAM287 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM287 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM287 are further described hereinbelow with reference to Table 1.

[3983] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM287 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3984] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 288 (VGAM288) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3985] VGAM288 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM288 was detected is described hereinabove with reference to Figs. 2-8.

[3986] VGAM288 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2.

VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[3987] VGAM288 gene, herein designated VGAM GENE, encodes a VGAM288 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM288 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM288 precursor RNA is designated SEQ ID:7474, and is provided hereinbelow with reference to the sequence listing part.

[3988] VGAM288 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[3989] An enzyme complex designated DICER COMPLEX, dices



the VGAM288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM288 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM288 RNA is designated SEQ ID:7475, and is provided hereinbelow with reference to the sequence listing part.

[3990] VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[3991] VGAM288 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM288 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM288 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[3992] The complementary binding of VGAM288 RNA, herein designated VGAM RNA, to host target binding sites on VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM288 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[3993] It is appreciated that VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM288 host target genes. The mRNA of each one of this plurality of VGAM288 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM288 RNA, herein designated VGAM RNA, and which when bound by VGAM288 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM288 host target proteins.

[3994] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM288 gene, herein designated VGAM GENE, on one or more VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[3995] It is yet further appreciated that a function of VGAM288 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM288 correlate with, and may be deduced from, the identity of the host target genes which VGAM288 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[3996] Nucleotide sequences of the VGAM288 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM288 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM288 are further described hereinbelow with reference to Table 1.

[3997] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM288 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[3998] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 289 (VGAM289) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[3999] VGAM289 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM289 was detected is described hereinabove with reference to Figs. 2-8.

[4000] VGAM289 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM289 host target gene, herein designated VGAM HOST TARGET

GENE, is a human gene contained in the human genome.

[4001] VGAM289 gene, herein designated VGAM GENE, encodes a VGAM289 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM289 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM289 precursor RNA is designated SEQ ID:7487, and is provided hereinbelow with reference to the sequence listing part.

[4002] VGAM289 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4003] An enzyme complex designated DICER COMPLEX, dices the VGAM289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM289 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM289 RNA is designated SEQ ID:7467, and is provided hereinbelow with reference to the sequence listing part.

[4004] VGAM289 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4005] VGAM289 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM289 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM289 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4006] The complementary binding of VGAM289 RNA, herein designated VGAM RNA, to host target binding sites on VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA,



into VGAM289 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4007] It is appreciated that VGAM289 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM289 host target genes. The mRNA of each one of this plurality of VGAM289 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM289 RNA, herein designated VGAM RNA, and which when bound by VGAM289 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM289 host target proteins.

[4008] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM289 gene, herein designated VGAM GENE, on one or more VGAM289 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4009] It is yet further appreciated that a function of VGAM289 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM289 correlate with, and may be deduced from, the identity of the host target genes which VGAM289 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4010] Nucleotide sequences of the VGAM289 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM289 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM289 are further de-

scribed hereinbelow with reference to Table 1.

[4011] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM289 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4012] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 290 (VGAM290) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4013] VGAM290 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM290 was detected is described hereinabove with reference to Figs. 2-8.

[4014] VGAM290 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4015] VGAM290 gene, herein designated VGAM GENE, encodes a

VGAM290 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM290 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM290 precursor RNA is designated SEQ ID:7488, and is provided hereinbelow with reference to the sequence listing part.

[4016] VGAM290 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4017] An enzyme complex designated DICER COMPLEX, dices the VGAM290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM290 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM290 RNA is designated SEQ ID:7489, and is provided hereinbelow with reference to the sequence listing part.

[4018] VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4019] VGAM290 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM290 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM290 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4020] The complementary binding of VGAM290 RNA, herein designated VGAM RNA, to host target binding sites on VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM290 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[4021] It is appreciated that VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM290 host target genes. The mRNA of each one of this plurality of VGAM290 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM290 RNA, herein designated VGAM RNA, and which when bound by VGAM290 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM290 host target proteins.

[4022] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM290 gene, herein designated VGAM GENE, on one or more VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4023] It is yet further appreciated that a function of VGAM290 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM290 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM290 correlate with, and may be deduced from, the identity of the host target genes which VGAM290 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4024] Nucleotide sequences of the VGAM290 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM290 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM290 are further described hereinbelow with reference to Table 1.

[4025] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM290 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4026] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 291 (VGAM291) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4027] VGAM291 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM291 was detected is described hereinabove with reference to Figs. 2-8.

[4028] VGAM291 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola virus. VGAM291 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4029] VGAM291 gene, herein designated VGAM GENE, encodes a VGAM291 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM291 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM291 precursor RNA is designated SEQ ID:7498, and is provided hereinbelow with reference to the sequence listing part.

[4030] VGAM291 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4031] An enzyme complex designated DICER COMPLEX, dices the VGAM291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM291 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM291 RNA is designated SEQ ID:7499, and is provided hereinbelow with reference to the sequence listing part.

[4032] VGAM291 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4033] VGAM291 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM291 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM291 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4034] The complementary binding of VGAM291 RNA, herein designated VGAM RNA, to host target binding sites on VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM291 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4035] It is appreciated that VGAM291 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM291 host target genes. The mRNA of each one of this plurality of VGAM291 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM291 RNA, herein designated VGAM RNA, and which when bound by VGAM291 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM291 host target proteins.

[4036] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM291 gene, herein designated VGAM GENE, on one or more VGAM291 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4037] It is yet further appreciated that a function of VGAM291 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM291 include diagnosis, prevention and treatment of viral infection by Variola virus. Specific functions, and accordingly utilities, of VGAM291 correlate with, and may be deduced from, the identity of the host target genes which VGAM291 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4038] Nucleotide sequences of the VGAM291 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM291 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM291 are further described hereinbelow with reference to Table 1.

[4039] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM291 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4040] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 292 (VGAM292) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4041] VGAM292 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM292 was detected is described hereinabove with reference to Figs. 2–8.

[4042] VGAM292 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4043] VGAM292 gene, herein designated VGAM GENE, encodes a VGAM292 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM292 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM292 precursor RNA is designated SEQ ID:7584, and is provided hereinbelow with reference to the sequence listing part.

[4044] VGAM292 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4045] An enzyme complex designated DICER COMPLEX, dices the VGAM292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM292 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other



necessary proteins. A probable (over 28%) nucleotide sequence of VGAM292 RNA is designated SEQ ID:7585, and is provided hereinbelow with reference to the sequence listing part.

[4046] VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4047] VGAM292 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM292 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4048] The complementary binding of VGAM292 RNA, herein designated VGAM RNA, to host target binding sites on VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM292 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4049] It is appreciated that VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM292 host target genes. The mRNA of each one of this plurality of VGAM292 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM292 RNA, herein designated VGAM RNA, and which when bound by VGAM292 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM292 host target proteins.

[4050] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM292 gene, herein designated VGAM GENE, on one or more VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[4051] It is yet further appreciated that a function of VGAM292 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM292 correlate with, and may be deduced from, the identity of the host target genes which VGAM292 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4052] Nucleotide sequences of the VGAM292 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM292 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM292 are further described hereinbelow with reference to Table 1.

[4053] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM292 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4054] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 293 (VGAM293) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4055] VGAM293 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM293 was detected is described hereinabove with reference to Figs. 2–8.

[4056] VGAM293 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM293 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4057] VGAM293 gene, herein designated VGAM GENE, encodes a VGAM293 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM293 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM293 precursor RNA is designated SEQ ID:7590, and is provided hereinbelow with reference to the sequence listing part.

[4058] VGAM293 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM293 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4059] An enzyme complex designated DICER COMPLEX, dices the VGAM293 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM293 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM293 RNA is designated SEQ ID:7591, and

is provided hereinbelow with reference to the sequence listing part.

[4060] VGAM293 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4061] VGAM293 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM293 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4062] The complementary binding of VGAM293 RNA, herein designated VGAM RNA, to host target binding sites on VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM293 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4063] It is appreciated that VGAM293 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM293 host target genes. The mRNA of each one of this plurality of VGAM293 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM293 RNA, herein designated VGAM RNA, and which when bound by VGAM293 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM293 host target proteins.

[4064] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM293 gene, herein designated VGAM GENE, on one or more VGAM293 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4065] It is yet further appreciated that a function of VGAM293 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM293 correlate with, and may be deduced from, the identity of the host target genes which VGAM293 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4066] Nucleotide sequences of the VGAM293 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM293 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM293 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM293 are further described hereinbelow with reference to Table 1.

[4067] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM293 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4068] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 294 (VGAM294) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4069] VGAM294 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM294 was detected is described hereinabove with reference to Figs. 2–8.

[4070] VGAM294 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4071] VGAM294 gene, herein designated VGAM GENE, encodes a VGAM294 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM294 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM294 precursor RNA is

designated SEQ ID:7605, and is provided hereinbelow with reference to the sequence listing part.

[4072] VGAM294 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4073] An enzyme complex designated DICER COMPLEX, dices the VGAM294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM294 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM294 RNA is designated SEQ ID:7606, and is provided hereinbelow with reference to the sequence

listing part.

[4074] VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4075] VGAM294 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM294 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM294 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4076] The complementary binding of VGAM294 RNA, herein designated VGAM RNA, to host target binding sites on VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM294 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4077] It is appreciated that VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM294 host target genes. The mRNA of each one of this plurality of VGAM294 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM294 RNA, herein designated VGAM RNA, and which when bound by VGAM294 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM294 host target proteins.

[4078] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM294 gene, herein designated VGAM GENE, on one or more VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4079] It is yet further appreciated that a function of VGAM294 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM294 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM294 correlate with, and may be deduced from, the identity of the host target genes which VGAM294 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4080] Nucleotide sequences of the VGAM294 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM294 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM294 are further described hereinbelow with reference to Table 1.

[4081] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM294 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4082] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 295 (VGAM295) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4083] VGAM295 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM295 was detected is described hereinabove with reference to Figs. 2–8.

[4084] VGAM295 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM295 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4085] VGAM295 gene, herein designated VGAM GENE, encodes a VGAM295 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM295 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM295 precursor RNA is designated SEQ ID:7617, and is provided hereinbelow with reference to the sequence listing part.

[4086] VGAM295 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4087] An enzyme complex designated DICER COMPLEX, dices the VGAM295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM295 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM295 RNA is designated SEQ ID:7618, and is provided hereinbelow with reference to the sequence listing part.

[4088] VGAM295 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4089] VGAM295 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM295 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM295 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4090] The complementary binding of VGAM295 RNA, herein designated VGAM RNA, to host target binding sites on VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM295 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4091] It is appreciated that VGAM295 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM295 host target genes. The mRNA of each one of this plurality of VGAM295 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM295 RNA, herein designated VGAM

RNA, and which when bound by VGAM295 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM295 host target proteins.

[4092] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM295 gene, herein designated VGAM GENE, on one or more VGAM295 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4093] It is yet further appreciated that a function of VGAM295 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM295 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM295 correlate with, and may be deduced from, the identity of the host target genes which VGAM295 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4094] Nucleotide sequences of the VGAM295 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM295 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM295 are further described hereinbelow with reference to Table 1.

[4095] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM295 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4096] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 296 (VGAM296) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4097] VGAM296 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM296 was detected is described hereinabove with reference to Figs. 2-8.

[4098] VGAM296 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM296 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4099] VGAM296 gene, herein designated VGAM GENE, encodes a

VGAM296 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM296 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM296 precursor RNA is designated SEQ ID:7636, and is provided hereinbelow with reference to the sequence listing part.

[4100] VGAM296 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4101] An enzyme complex designated DICER COMPLEX, dices the VGAM296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM296 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM296 RNA is designated SEQ ID:7637, and is provided hereinbelow with reference to the sequence listing part.

[4102] VGAM296 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4103] VGAM296 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM296 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM296 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4104] The complementary binding of VGAM296 RNA, herein designated VGAM RNA, to host target binding sites on VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM296 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[4105] It is appreciated that VGAM296 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM296 host target genes. The mRNA of each one of this plurality of VGAM296 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM296 RNA, herein designated VGAM RNA, and which when bound by VGAM296 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM296 host target proteins.

[4106] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM296 gene, herein designated VGAM GENE, on one or more VGAM296 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4107] It is yet further appreciated that a function of VGAM296 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM296 include diagnosis, prevention and treatment of viral infection by Mollusum contagiosum virus. Specific functions, and accordingly utilities, of VGAM296 correlate with, and may be deduced from, the identity of the host target genes which VGAM296 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4108] Nucleotide sequences of the VGAM296 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM296 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM296 are further described hereinbelow with reference to Table 1.

[4109] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM296 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4110] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 297 (VGAM297) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4111] VGAM297 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM297 was detected is described hereinabove with reference to Figs. 2-8.

[4112] VGAM297 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4113] VGAM297 gene, herein designated VGAM GENE, encodes a VGAM297 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM297 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM297 precursor RNA is designated SEQ ID:7749, and is provided hereinbelow with reference to the sequence listing part.

[4114] VGAM297 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4115] An enzyme complex designated DICER COMPLEX, dices the VGAM297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM297 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM297 RNA is designated SEQ ID:7750, and is provided hereinbelow with reference to the sequence listing part.

[4116] VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4117] VGAM297 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM297 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4118] The complementary binding of VGAM297 RNA, herein designated VGAM RNA, to host target binding sites on VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM297 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[4119] It is appreciated that VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM297 host target genes. The mRNA of each one of this plurality of VGAM297 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM297 RNA, herein designated VGAM RNA, and which when bound by VGAM297 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM297 host target proteins.

[4120] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM297 gene, herein designated VGAM GENE, on one or more VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4121] It is yet further appreciated that a function of VGAM297 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM297 correlate with, and may be deduced from, the identity of the host target genes which VGAM297 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4122] Nucleotide sequences of the VGAM297 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM297 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM297 are further described hereinbelow with reference to Table 1.

[4123] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM297 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4124] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 298 (VGAM298) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4125] VGAM298 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM298 was detected is described hereinabove with reference to Figs. 2–8.

[4126] VGAM298 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM298 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4127] VGAM298 gene, herein designated VGAM GENE, encodes a VGAM298 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM298 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM298 precursor RNA is designated SEQ ID:7756, and is provided hereinbelow with reference to the sequence listing part.

[4128] VGAM298 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4129] An enzyme complex designated DICER COMPLEX, dices the VGAM298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM298 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM298 RNA is designated SEQ ID:7757, and is provided hereinbelow with reference to the sequence listing part.

[4130] VGAM298 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4131] VGAM298 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM298 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4132] The complementary binding of VGAM298 RNA, herein designated VGAM RNA, to host target binding sites on VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM298 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4133] It is appreciated that VGAM298 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM298 host target genes. The mRNA of each one of this plurality of VGAM298 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM298 RNA, herein designated VGAM RNA, and which when bound by VGAM298 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM298 host target proteins.

[4134] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM298 gene, herein designated VGAM GENE, on one or more VGAM298 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[4135] It is yet further appreciated that a function of VGAM298 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM298 correlate with, and may be deduced from, the identity of the host target genes which VGAM298 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[4136] Nucleotide sequences of the VGAM298 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM298 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM298 are further described hereinbelow with reference to Table 1.

[4137] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM298 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4138] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 299 (VGAM299) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4139] VGAM299 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM299 was detected is described hereinabove with reference to Figs. 2–8.

[4140] VGAM299 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM299 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4141] VGAM299 gene, herein designated VGAM GENE, encodes a VGAM299 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM299 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM299 precursor RNA is designated SEQ ID:7769, and is provided hereinbelow with reference to the sequence listing part.

[4142] VGAM299 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4143] An enzyme complex designated DICER COMPLEX, dices the VGAM299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM299 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM299 RNA is designated SEQ ID:7770, and is provided hereinbelow with reference to the sequence listing part.

[4144] VGAM299 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4145] VGAM299 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM299 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4146] The complementary binding of VGAM299 RNA, herein designated VGAM RNA, to host target binding sites on VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM299 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4147] It is appreciated that VGAM299 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM299 host target genes. The mRNA of

each one of this plurality of VGAM299 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM299 RNA, herein designated VGAM RNA, and which when bound by VGAM299 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM299 host target proteins.

[4148] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM299 gene, herein designated VGAM GENE, on one or more VGAM299 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[4149] It is yet further appreciated that a function of VGAM299 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM299 correlate with, and may be deduced from, the identity of the host target genes which VGAM299 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4150] Nucleotide sequences of the VGAM299 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM299 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM299 are further described hereinbelow with reference to Table 1.

[4151] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM299 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[4152] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 300 (VGAM300) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4153] VGAM300 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM300 was detected is described hereinabove with reference to Figs. 2–8.

[4154] VGAM300 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4155] VGAM300 gene, herein designated VGAM GENE, encodes a VGAM300 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM300 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM300 precursor RNA is

designated SEQ ID:7781, and is provided hereinbelow with reference to the sequence listing part.

[4156] VGAM300 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4157] An enzyme complex designated DICER COMPLEX, dices the VGAM300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM300 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM300 RNA is designated SEQ ID:7467, and is provided hereinbelow with reference to the sequence



listing part.

[4158] VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4159] VGAM300 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM300 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4160] The complementary binding of VGAM300 RNA, herein designated VGAM RNA, to host target binding sites on VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM300 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4161] It is appreciated that VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM300 host target genes. The mRNA of each one of this plurality of VGAM300 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM300 RNA, herein designated VGAM RNA, and which when bound by VGAM300 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM300 host target proteins.

[4162] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM300 gene, herein designated VGAM GENE, on one or more VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4163] It is yet further appreciated that a function of VGAM300 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM300 correlate with, and may be deduced from, the identity of the host target genes which VGAM300 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[4164] Nucleotide sequences of the VGAM300 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM300 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM300 are further described hereinbelow with reference to Table 1.

[4165] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM300 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4166] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 301 (VGAM301) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4167] VGAM301 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM301 was detected is described hereinabove with reference to Figs. 2–8.

[4168] VGAM301 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4169] VGAM301 gene, herein designated VGAM GENE, encodes a VGAM301 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM301 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM301 precursor RNA is designated SEQ ID:7782, and is provided hereinbelow with

reference to the sequence listing part.

[4170] VGAM301 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM301 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4171] An enzyme complex designated DICER COMPLEX, dices the VGAM301 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM301 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM301 RNA is designated SEQ ID:7783, and is provided hereinbelow with reference to the sequence listing part.

[4172] VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4173] VGAM301 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM301 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM301 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4174] The complementary binding of VGAM301 RNA, herein designated VGAM RNA, to host target binding sites on VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM301 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4175] It is appreciated that VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM301 host target genes. The mRNA of each one of this plurality of VGAM301 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM301 RNA, herein designated VGAM RNA, and which when bound by VGAM301 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM301 host target proteins.

[4176] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM301 gene, herein designated VGAM GENE, on one or more VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4177] It is yet further appreciated that a function of VGAM301 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM301 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM301 correlate with, and may be deduced from, the identity of the host target genes which VGAM301 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4178] Nucleotide sequences of the VGAM301 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM301 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM301 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM301 are further described hereinbelow with reference to Table 1.

[4179] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM301 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4180] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 302 (VGAM302) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4181] VGAM302 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM302 was detected is described hereinabove with reference to Figs. 2–8.

[4182] VGAM302 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM302 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4183] VGAM302 gene, herein designated VGAM GENE, encodes a VGAM302 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM302 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM302 precursor RNA is designated SEQ ID:7801, and is provided hereinbelow with reference to the sequence listing part.

[4184] VGAM302 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4185] An enzyme complex designated DICER COMPLEX, dices the VGAM302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM302 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM302 RNA is designated SEQ ID:7802, and is provided hereinbelow with reference to the sequence listing part.

[4186] VGAM302 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4187] VGAM302 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM302 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4188] The complementary binding of VGAM302 RNA, herein designated VGAM RNA, to host target binding sites on VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM302 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4189] It is appreciated that VGAM302 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM302 host target genes. The mRNA of each one of this plurality of VGAM302 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM302 RNA, herein designated VGAM

RNA, and which when bound by VGAM302 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM302 host target proteins.

[4190] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM302 gene, herein designated VGAM GENE, on one or more VGAM302 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4191] It is yet further appreciated that a function of VGAM302 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM302 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM302 correlate with, and may be deduced from, the identity of the host target genes which VGAM302 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4192] Nucleotide sequences of the VGAM302 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM302 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM302 are further described hereinbelow with reference to Table 1.

[4193] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM302 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4194] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 303 (VGAM303) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4195] VGAM303 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM303 was detected is described hereinabove with reference to Figs. 2–8.

[4196] VGAM303 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4197] VGAM303 gene, herein designated VGAM GENE, encodes a VGAM303 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM303 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM303 precursor RNA is designated SEQ ID:7809, and is provided hereinbelow with reference to the sequence listing part.

[4198] VGAM303 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4199] An enzyme complex designated DICER COMPLEX, dices the VGAM303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM303 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM303 RNA is designated SEQ ID:7810, and is provided hereinbelow with reference to the sequence listing part.

[4200] VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4201] VGAM303 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM303 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM303 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM303 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4202] The complementary binding of VGAM303 RNA, herein designated VGAM RNA, to host target binding sites on VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM303 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4203] It is appreciated that VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM303 host target genes. The mRNA of each one of this plurality of VGAM303 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM303 RNA, herein designated VGAM RNA, and which when bound by VGAM303 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM303 host target proteins.

[4204] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM303 gene, herein designated VGAM GENE, on one or more VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4205] It is yet further appreciated that a function of VGAM303 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM303 include diagnosis, prevention and

treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM303 correlate with, and may be deduced from, the identity of the host target genes which VGAM303 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4206] Nucleotide sequences of the VGAM303 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM303 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM303 are further described hereinbelow with reference to Table 1.

[4207] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM303 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4208] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 304 (VGAM304) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4209] VGAM304 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM304 was detected is described hereinabove with reference to Figs. 2–8.

[4210] VGAM304 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM304 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4211] VGAM304 gene, herein designated VGAM GENE, encodes a VGAM304 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM304 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM304 precursor RNA is designated SEQ ID:7815, and is provided hereinbelow with reference to the sequence listing part.

[4212] VGAM304 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM304 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4213] An enzyme complex designated DICER COMPLEX, dices the VGAM304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM304 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM304 RNA is designated SEQ ID:7816, and is provided hereinbelow with reference to the sequence listing part.

[4214] VGAM304 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM304 host target RNA, herein designated VGAM



HOST TARGET RNA. VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4215] VGAM304 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM304 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4216] The complementary binding of VGAM304 RNA, herein designated VGAM RNA, to host target binding sites on VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM304 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4217] It is appreciated that VGAM304 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM304 host target genes. The mRNA of each one of this plurality of VGAM304 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM304 RNA, herein designated VGAM RNA, and which when bound by VGAM304 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM304 host target proteins.

[4218] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM304 gene, herein designated VGAM GENE, on one or more VGAM304 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4219] It is yet further appreciated that a function of VGAM304 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Spe-

cific functions, and accordingly utilities, of VGAM304 correlate with, and may be deduced from, the identity of the host target genes which VGAM304 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4220] Nucleotide sequences of the VGAM304 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM304 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM304 are further described hereinbelow with reference to Table 1.

[4221] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM304 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4222] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 305 (VGAM305) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[4223] VGAM305 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM305 was detected is described hereinabove with reference to Figs. 2–8.

[4224] VGAM305 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4225] VGAM305 gene, herein designated VGAM GENE, encodes a VGAM305 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM305 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM305 precursor RNA is designated SEQ ID:7822, and is provided hereinbelow with reference to the sequence listing part.

[4226] VGAM305 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM305 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4227] An enzyme complex designated DICER COMPLEX, dices the VGAM305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM305 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM305 RNA is designated SEQ ID:7823, and is provided hereinbelow with reference to the sequence listing part.

[4228] VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM305 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4229] VGAM305 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM305 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM305 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4230] The complementary binding of VGAM305 RNA, herein designated VGAM RNA, to host target binding sites on VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM305 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4231] It is appreciated that VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM305 host target genes. The mRNA of each one of this plurality of VGAM305 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM305 RNA, herein designated VGAM RNA, and which when bound by VGAM305 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM305 host target proteins.



[4232] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM305 gene, herein designated VGAM GENE, on one or more VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4233] It is yet further appreciated that a function of VGAM305 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM305 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM305 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM305 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4234] Nucleotide sequences of the VGAM305 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM305 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM305 are further described hereinbelow with reference to Table 1.

[4235] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM305 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4236] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 306 (VGAM306) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[4237] VGAM306 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM306 was detected is described hereinabove with reference to Figs. 2–8.

[4238] VGAM306 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4239] VGAM306 gene, herein designated VGAM GENE, encodes a VGAM306 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM306 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM306 precursor RNA is designated SEQ ID:7834, and is provided hereinbelow with reference to the sequence listing part.

[4240] VGAM306 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4241] An enzyme complex designated DICER COMPLEX, dices the VGAM306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM306 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM306 RNA is designated SEQ ID:7835, and is provided hereinbelow with reference to the sequence listing part.

[4242] VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4243] VGAM306 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM306 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4244] The complementary binding of VGAM306 RNA, herein designated VGAM RNA, to host target binding sites on VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM306 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4245] It is appreciated that VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM306 host target genes. The mRNA of each one of this plurality of VGAM306 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM306 RNA, herein designated VGAM RNA, and which when bound by VGAM306 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM306 host target proteins.

[4246] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM306 gene, herein designated VGAM GENE, on one or more VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4247] It is yet further appreciated that a function of VGAM306 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM306 correlate with, and may be deduced from, the identity of the

host target genes which VGAM306 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4248] Nucleotide sequences of the VGAM306 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM306 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM306 are further described hereinbelow with reference to Table 1.

[4249] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM306 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4250] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 307 (VGAM307) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[4251] VGAM307 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM307 was detected is described hereinabove with reference to Figs. 2–8.

[4252] VGAM307 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4253] VGAM307 gene, herein designated VGAM GENE, encodes a VGAM307 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM307 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM307 precursor RNA is designated SEQ ID:7845, and is provided hereinbelow with reference to the sequence listing part.

[4254] VGAM307 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4255] An enzyme complex designated DICER COMPLEX, dices the VGAM307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM307 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM307 RNA is designated SEQ ID:7467, and is provided hereinbelow with reference to the sequence listing part.

[4256] VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4257] VGAM307 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM307 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM307 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[4258] The complementary binding of VGAM307 RNA, herein designated VGAM RNA, to host target binding sites on VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM307 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4259] It is appreciated that VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM307 host target genes. The mRNA of each one of this plurality of VGAM307 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM307 RNA, herein designated VGAM RNA, and which when bound by VGAM307 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM307 host target proteins.

[4260] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM307 gene, herein designated VGAM GENE, on one or more VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4261] It is yet further appreciated that a function of VGAM307 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM307 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM307 correlate with, and may be deduced from, the identity of the host target genes which VGAM307 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[4262] Nucleotide sequences of the VGAM307 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM307 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM307 are further described hereinbelow with reference to Table 1.

[4263] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM307 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4264] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 308 (VGAM308) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4265] VGAM308 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM308 was detected is described hereinabove with reference to Figs. 2–8.

[4266] VGAM308 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4267] VGAM308 gene, herein designated VGAM GENE, encodes a VGAM308 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM308 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM308 precursor RNA is designated SEQ ID:7846, and is provided hereinbelow with reference to the sequence listing part.

[4268] VGAM308 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4269] An enzyme complex designated DICER COMPLEX, dices the VGAM308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM308 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM308 RNA is designated SEQ ID:7847, and is provided hereinbelow with reference to the sequence listing part.

[4270] VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and



3UTR respectively.

[4271] VGAM308 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM308 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM308 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4272] The complementary binding of VGAM308 RNA, herein designated VGAM RNA, to host target binding sites on VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM308 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4273] It is appreciated that VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM308 host target genes. The mRNA of each one of this plurality of VGAM308 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM308 RNA, herein designated VGAM RNA, and which when bound by VGAM308 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM308 host target proteins.

[4274] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM308 gene, herein designated VGAM GENE, on one or

more VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4275] It is yet further appreciated that a function of VGAM308 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM308 include diagnosis, prevention and treatment of viral infection by Molluscum contagiosum virus. Specific functions, and accordingly utilities, of VGAM308 correlate with, and may be deduced from, the identity of the host target genes which VGAM308 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4276] Nucleotide sequences of the VGAM308 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM308 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM308 are further described hereinbelow with reference to Table 1.

[4277] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM308 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4278] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 309 (VGAM309) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4279] VGAM309 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM309 was detected is described

hereinabove with reference to Figs. 2–8.

[4280] VGAM309 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM309 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4281] VGAM309 gene, herein designated VGAM GENE, encodes a VGAM309 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM309 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM309 precursor RNA is designated SEQ ID:7855, and is provided hereinbelow with reference to the sequence listing part.

[4282] VGAM309 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4283] An enzyme complex designated DICER COMPLEX, dices the VGAM309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM309 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM309 RNA is designated SEQ ID:7856, and is provided hereinbelow with reference to the sequence listing part.

[4284] VGAM309 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4285] VGAM309 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM309 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4286] The complementary binding of VGAM309 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM309 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4287] It is appreciated that VGAM309 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM309 host target genes. The mRNA of each one of this plurality of VGAM309 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM309 RNA, herein designated VGAM RNA, and which when bound by VGAM309 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM309 host target proteins.

[4288] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM309 gene, herein designated VGAM GENE, on one or more VGAM309 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4289] It is yet further appreciated that a function of VGAM309 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM309 correlate with, and may be deduced from, the identity of the host target genes which VGAM309 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4290] Nucleotide sequences of the VGAM309 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM309 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM309 are further described hereinbelow with reference to Table 1.

[4291] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM309 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4292] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 310 (VGAM310) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4293] VGAM310 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM310 was detected is described hereinabove with reference to Figs. 2-8.

[4294] VGAM310 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4295] VGAM310 gene, herein designated VGAM GENE, encodes a VGAM310 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM310 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM310 precursor RNA is designated SEQ ID:7919, and is provided hereinbelow with reference to the sequence listing part.

[4296] VGAM310 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4297] An enzyme complex designated DICER COMPLEX, dices the VGAM310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM310 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM310 RNA is designated SEQ ID:7920, and is provided hereinbelow with reference to the sequence listing part.

[4298] VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4299] VGAM310 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM310 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4300] The complementary binding of VGAM310 RNA, herein designated VGAM RNA, to host target binding sites on VGAM310 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM310 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4301] It is appreciated that VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM310 host target genes. The mRNA of each one of this plurality of VGAM310 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM310 RNA, herein designated VGAM RNA, and which when bound by VGAM310 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM310 host target proteins.

[4302] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM310 gene, herein designated VGAM GENE, on one or more VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4303] It is yet further appreciated that a function of VGAM310 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM310 correlate with, and may be deduced from, the identity of the host target genes which VGAM310 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4304] Nucleotide sequences of the VGAM310 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM310 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM310 are further described hereinbelow with reference to Table 1.

[4305] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM310 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4306] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 311 (VGAM311) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4307] VGAM311 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM311 was detected is described hereinabove with reference to Figs. 2-8.

[4308] VGAM311 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2.



VGAM311 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4309] VGAM311 gene, herein designated VGAM GENE, encodes a VGAM311 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM311 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM311 precursor RNA is designated SEQ ID:7927, and is provided hereinbelow with reference to the sequence listing part.

[4310] VGAM311 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4311] An enzyme complex designated DICER COMPLEX, dices

the VGAM311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM311 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM311 RNA is designated SEQ ID:7928, and is provided hereinbelow with reference to the sequence listing part.

[4312] VGAM311 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4313] VGAM311 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM311 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM311 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4314] The complementary binding of VGAM311 RNA, herein designated VGAM RNA, to host target binding sites on VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM311 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4315] It is appreciated that VGAM311 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM311 host target genes. The mRNA of each one of this plurality of VGAM311 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM311 RNA, herein designated VGAM RNA, and which when bound by VGAM311 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM311 host target proteins.

[4316] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM311 gene, herein designated VGAM GENE, on one or more VGAM311 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4317] It is yet further appreciated that a function of VGAM311 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM311 correlate with, and may be deduced from, the identity of the host target genes which VGAM311 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4318] Nucleotide sequences of the VGAM311 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM311 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM311 are further described hereinbelow with reference to Table 1.

[4319] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM311 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4320] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 312 (VGAM312) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4321] VGAM312 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM312 was detected is described hereinabove with reference to Figs. 2-8.

[4322] VGAM312 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM312 host target gene, herein designated VGAM HOST TARGET

GENE, is a human gene contained in the human genome.

[4323] VGAM312 gene, herein designated VGAM GENE, encodes a VGAM312 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM312 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM312 precursor RNA is designated SEQ ID:7993, and is provided hereinbelow with reference to the sequence listing part.

[4324] VGAM312 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4325] An enzyme complex designated DICER COMPLEX, dices the VGAM312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM312 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM312 RNA is designated SEQ ID:7195, and is provided hereinbelow with reference to the sequence listing part.

[4326] VGAM312 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4327] VGAM312 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM312 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM312 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4328] The complementary binding of VGAM312 RNA, herein designated VGAM RNA, to host target binding sites on VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM312 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4329] It is appreciated that VGAM312 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM312 host target genes. The mRNA of each one of this plurality of VGAM312 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM312 RNA, herein designated VGAM RNA, and which when bound by VGAM312 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM312 host target proteins.

[4330] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM312 gene, herein designated VGAM GENE, on one or more VGAM312 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4331] It is yet further appreciated that a function of VGAM312 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM312 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM312 correlate with, and may be deduced from, the identity of the host target genes which VGAM312 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4332] Nucleotide sequences of the VGAM312 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM312 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM312 are further de-

scribed hereinbelow with reference to Table 1.

[4333] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM312 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4334] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 313 (VGAM313) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4335] VGAM313 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM313 was detected is described hereinabove with reference to Figs. 2-8.

[4336] VGAM313 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM313 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4337] VGAM313 gene, herein designated VGAM GENE, encodes a VGAM313 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM313 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM313 precursor RNA is designated SEQ ID:7994, and is provided hereinbelow with reference to the sequence listing part.

[4338] VGAM313 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4339] An enzyme complex designated DICER COMPLEX, dices the VGAM313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM313 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM313 RNA is designated SEQ ID:7995, and is provided hereinbelow with reference to the sequence listing part.

[4340] VGAM313 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4341] VGAM313 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM313 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM313 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4342] The complementary binding of VGAM313 RNA, herein designated VGAM RNA, to host target binding sites on VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM313 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4343] It is appreciated that VGAM313 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM313 host target genes. The mRNA of each one of this plurality of VGAM313 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM313 RNA, herein designated VGAM RNA, and which when bound by VGAM313 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM313 host target proteins.

[4344] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM313 gene, herein designated VGAM GENE, on one or more VGAM313 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4345] It is yet further appreciated that a function of VGAM313 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM313 correlate with, and may be deduced from, the identity of the host target genes which VGAM313 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4346] Nucleotide sequences of the VGAM313 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM313 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM313 are further described hereinbelow with reference to Table 1.

[4347] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM313 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4348] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 314 (VGAM314) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4349] VGAM314 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM314 was detected is described hereinabove with reference to Figs. 2-8.

[4350] VGAM314 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4351] VGAM314 gene, herein designated VGAM GENE, encodes a

VGAM314 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM314 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM314 precursor RNA is designated SEQ ID:8069, and is provided hereinbelow with reference to the sequence listing part.

[4352] VGAM314 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4353] An enzyme complex designated DICER COMPLEX, dices the VGAM314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM314 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM314 RNA is designated SEQ ID:8070, and is provided hereinbelow with reference to the sequence listing part.

[4354] VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4355] VGAM314 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM314 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4356] The complementary binding of VGAM314 RNA, herein designated VGAM RNA, to host target binding sites on VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM314 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[4357] It is appreciated that VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM314 host target genes. The mRNA of each one of this plurality of VGAM314 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM314 RNA, herein designated VGAM RNA, and which when bound by VGAM314 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM314 host target proteins.

[4358] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM314 gene, herein designated VGAM GENE, on one or more VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4359] It is yet further appreciated that a function of VGAM314 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM314 correlate with, and may be deduced from, the identity of the host target genes which VGAM314 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4360] Nucleotide sequences of the VGAM314 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM314 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM314 are further described hereinbelow with reference to Table 1.

[4361] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM314 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4362] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 315 (VGAM315) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4363] VGAM315 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM315 was detected is described hereinabove with reference to Figs. 2-8.

[4364] VGAM315 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lactate dehydrogenase-elevating virus. VGAM315 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4365] VGAM315 gene, herein designated VGAM GENE, encodes a VGAM315 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM315 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM315 precursor RNA is designated SEQ ID:8111, and is provided hereinbelow with reference to the sequence listing part.

[4366] VGAM315 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4367] An enzyme complex designated DICER COMPLEX, dices the VGAM315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM315 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM315 RNA is designated SEQ ID:8112, and is provided hereinbelow with reference to the sequence listing part.

[4368] VGAM315 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4369] VGAM315 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM315 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4370] The complementary binding of VGAM315 RNA, herein designated VGAM RNA, to host target binding sites on VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM315 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4371] It is appreciated that VGAM315 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM315 host target genes. The mRNA of each one of this plurality of VGAM315 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM315 RNA, herein designated VGAM RNA, and which when bound by VGAM315 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM315 host target proteins.

[4372] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM315 gene, herein designated VGAM GENE, on one or more VGAM315 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4373] It is yet further appreciated that a function of VGAM315 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of viral infection by Lactate dehydrogenase-elevating virus. Specific functions, and accordingly utilities, of VGAM315 correlate with, and may be deduced from, the identity of the host target genes which VGAM315 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4374] Nucleotide sequences of the VGAM315 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM315 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM315 are further described hereinbelow with reference to Table 1.

[4375] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM315 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4376] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 316 (VGAM316) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4377] VGAM316 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM316 was detected is described hereinabove with reference to Figs. 2–8.

[4378] VGAM316 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM316 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4379] VGAM316 gene, herein designated VGAM GENE, encodes a VGAM316 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM316 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM316 precursor RNA is designated SEQ ID:8121, and is provided hereinbelow with reference to the sequence listing part.

[4380] VGAM316 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4381] An enzyme complex designated DICER COMPLEX, dices the VGAM316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM316 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM316 RNA is designated SEQ ID:8122, and is provided hereinbelow with reference to the sequence listing part.

[4382] VGAM316 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4383] VGAM316 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM316 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4384] The complementary binding of VGAM316 RNA, herein designated VGAM RNA, to host target binding sites on VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM316 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4385] It is appreciated that VGAM316 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM316 host target genes. The mRNA of each one of this plurality of VGAM316 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM316 RNA, herein designated VGAM RNA, and which when bound by VGAM316 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM316 host target proteins.

[4386] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM316 gene, herein designated VGAM GENE, on one or more VGAM316 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4387] It is yet further appreciated that a function of VGAM316 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM316 correlate with, and may be deduced from, the identity of the host target genes which VGAM316 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4388] Nucleotide sequences of the VGAM316 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM316 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM316 are further described hereinbelow with reference to Table 1.

[4389] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM316 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4390] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 317 (VGAM317) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4391] VGAM317 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM317 was detected is described hereinabove with reference to Figs. 2–8.

[4392] VGAM317 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM317 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4393] VGAM317 gene, herein designated VGAM GENE, encodes a VGAM317 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM317 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM317 precursor RNA is designated SEQ ID:8142, and is provided hereinbelow with reference to the sequence listing part.

[4394] VGAM317 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4395] An enzyme complex designated DICER COMPLEX, dices the VGAM317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM317 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 55%) nucleotide sequence of VGAM317 RNA is designated SEQ ID:8143, and is provided hereinbelow with reference to the sequence listing part.

[4396] VGAM317 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4397] VGAM317 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM317 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4398] The complementary binding of VGAM317 RNA, herein designated VGAM RNA, to host target binding sites on VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM317 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4399] It is appreciated that VGAM317 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM317 host target genes. The mRNA of each one of this plurality of VGAM317 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM317 RNA, herein designated VGAM RNA, and which when bound by VGAM317 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM317 host target proteins.

[4400] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM317 gene, herein designated VGAM GENE, on one or more VGAM317 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[4401] It is yet further appreciated that a function of VGAM317 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM317 correlate with, and may be deduced from, the identity of the host target genes which VGAM317 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4402] Nucleotide sequences of the VGAM317 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM317 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM317 are further described hereinbelow with reference to Table 1.

[4403] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM317 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4404] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 318 (VGAM318) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4405] VGAM318 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM318 was detected is described hereinabove with reference to Figs. 2–8.

[4406] VGAM318 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lactate dehydrogenase–elevating virus. VGAM318 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4407] VGAM318 gene, herein designated VGAM GENE, encodes a VGAM318 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM318 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM318 precursor RNA is designated SEQ ID:8165, and is provided hereinbelow with reference to the sequence listing part.

[4408] VGAM318 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4409] An enzyme complex designated DICER COMPLEX, dices the VGAM318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM318 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM318 RNA is designated SEQ ID:8166, and is provided hereinbelow with reference to the sequence listing part.

[4410] VGAM318 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4411] VGAM318 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM318 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4412] The complementary binding of VGAM318 RNA, herein designated VGAM RNA, to host target binding sites on VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM318 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4413] It is appreciated that VGAM318 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM318 host target genes. The mRNA of

each one of this plurality of VGAM318 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM318 RNA, herein designated VGAM RNA, and which when bound by VGAM318 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM318 host target proteins.

[4414] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM318 gene, herein designated VGAM GENE, on one or more VGAM318 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

- [4415] It is yet further appreciated that a function of VGAM318 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of viral infection by Lactate dehydrogenase-elevating virus. Specific functions, and accordingly utilities, of VGAM318 correlate with, and may be deduced from, the identity of the host target genes which VGAM318 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [4416] Nucleotide sequences of the VGAM318 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM318 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM318 are further described hereinbelow with reference to Table 1.
- [4417] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM318 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[4418] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 319 (VGAM319) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4419] VGAM319 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM319 was detected is described hereinabove with reference to Figs. 2–8.

[4420] VGAM319 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4421] VGAM319 gene, herein designated VGAM GENE, encodes a VGAM319 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM319 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar



to the nucleotide sequence of VGAM319 precursor RNA is designated SEQ ID:8172, and is provided hereinbelow with reference to the sequence listing part.

[4422] VGAM319 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4423] An enzyme complex designated DICER COMPLEX, dices the VGAM319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM319 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM319 RNA is designated SEQ ID:8173, and

is provided hereinbelow with reference to the sequence listing part.

[4424] VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4425] VGAM319 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM319 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM319 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4426] The complementary binding of VGAM319 RNA, herein designated VGAM RNA, to host target binding sites on VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM319 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4427] It is appreciated that VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM319 host target genes. The mRNA of each one of this plurality of VGAM319 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM319 RNA, herein designated VGAM RNA, and which when bound by VGAM319 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM319 host target proteins.

[4428] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM319 gene, herein designated VGAM GENE, on one or more VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4429] It is yet further appreciated that a function of VGAM319 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM319 correlate with, and may be deduced from, the identity of the host target genes which VGAM319 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4430] Nucleotide sequences of the VGAM319 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM319 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM319 are further described hereinbelow with reference to Table 1.

[4431] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM319 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4432] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 320 (VGAM320) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4433] VGAM320 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM320 was detected is described hereinabove with reference to Figs. 2–8.

[4434] VGAM320 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4435] VGAM320 gene, herein designated VGAM GENE, encodes a VGAM320 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM320 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM320 precursor RNA is

designated SEQ ID:8215, and is provided hereinbelow with reference to the sequence listing part.

[4436] VGAM320 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4437] An enzyme complex designated DICER COMPLEX, dices the VGAM320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM320 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM320 RNA is designated SEQ ID:8216, and is provided hereinbelow with reference to the sequence

listing part.

[4438] VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4439] VGAM320 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM320 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM320 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4440] The complementary binding of VGAM320 RNA, herein designated VGAM RNA, to host target binding sites on VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM320 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4441] It is appreciated that VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM320 host target genes. The mRNA of each one of this plurality of VGAM320 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM320 RNA, herein designated VGAM RNA, and which when bound by VGAM320 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM320 host target proteins.

[4442] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM320 gene, herein designated VGAM GENE, on one or more VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4443] It is yet further appreciated that a function of VGAM320 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM320 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM320 correlate with, and may be deduced from, the identity of the host target genes which VGAM320 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4444] Nucleotide sequences of the VGAM320 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM320 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM320 are further described hereinbelow with reference to Table 1.

[4445] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM320 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4446] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 321 (VGAM321) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4447] VGAM321 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM321 was detected is described hereinabove with reference to Figs. 2–8.

[4448] VGAM321 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4449] VGAM321 gene, herein designated VGAM GENE, encodes a VGAM321 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM321 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM321 precursor RNA is designated SEQ ID:8292, and is provided hereinbelow with

reference to the sequence listing part.

[4450] VGAM321 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4451] An enzyme complex designated DICER COMPLEX, dices the VGAM321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM321 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM321 RNA is designated SEQ ID:8293, and is provided hereinbelow with reference to the sequence listing part.

[4452] VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4453] VGAM321 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM321 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4454] The complementary binding of VGAM321 RNA, herein designated VGAM RNA, to host target binding sites on VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM321 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4455] It is appreciated that VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM321 host target genes. The mRNA of each one of this plurality of VGAM321 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM321 RNA, herein designated VGAM RNA, and which when bound by VGAM321 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM321 host target proteins.

[4456] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM321 gene, herein designated VGAM GENE, on one or more VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4457] It is yet further appreciated that a function of VGAM321 is inhibition of expression of host target genes, as part of a



novel viral mechanism of attacking a host. Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM321 correlate with, and may be deduced from, the identity of the host target genes which VGAM321 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4458] Nucleotide sequences of the VGAM321 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM321 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM321 are further described hereinbelow with reference to Table 1.

[4459] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM321 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4460] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 322 (VGAM322) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4461] VGAM322 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM322 was detected is described hereinabove with reference to Figs. 2–8.

[4462] VGAM322 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM322 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4463] VGAM322 gene, herein designated VGAM GENE, encodes a VGAM322 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM322 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM322 precursor RNA is designated SEQ ID:8304, and is provided hereinbelow with reference to the sequence listing part.

[4464] VGAM322 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4465] An enzyme complex designated DICER COMPLEX, dices the VGAM322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM322 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM322 RNA is designated SEQ ID:8305, and is provided hereinbelow with reference to the sequence listing part.

[4466] VGAM322 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4467] VGAM322 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM322 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4468] The complementary binding of VGAM322 RNA, herein designated VGAM RNA, to host target binding sites on VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM322 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4469] It is appreciated that VGAM322 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM322 host target genes. The mRNA of each one of this plurality of VGAM322 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM322 RNA, herein designated VGAM

RNA, and which when bound by VGAM322 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM322 host target proteins.

[4470] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM322 gene, herein designated VGAM GENE, on one or more VGAM322 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4471] It is yet further appreciated that a function of VGAM322 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM322 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM322 correlate with, and may be deduced from, the identity of the host target genes which VGAM322 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4472] Nucleotide sequences of the VGAM322 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM322 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM322 are further described hereinbelow with reference to Table 1.

[4473] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM322 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4474] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 323 (VGAM323) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4475] VGAM323 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM323 was detected is described hereinabove with reference to Figs. 2–8.

[4476] VGAM323 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM323 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4477] VGAM323 gene, herein designated VGAM GENE, encodes a VGAM323 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM323 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM323 precursor RNA is designated SEQ ID:8313, and is provided hereinbelow with reference to the sequence listing part.

[4478] VGAM323 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4479] An enzyme complex designated DICER COMPLEX, dices the VGAM323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM323 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM323 RNA is designated SEQ ID:8314, and is provided hereinbelow with reference to the sequence listing part.

[4480] VGAM323 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4481] VGAM323 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM323 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM323 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4482] The complementary binding of VGAM323 RNA, herein designated VGAM RNA, to host target binding sites on VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM323 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4483] It is appreciated that VGAM323 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM323 host target genes. The mRNA of each one of this plurality of VGAM323 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM323 RNA, herein designated VGAM RNA, and which when bound by VGAM323 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM323 host target proteins.

[4484] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM323 gene, herein designated VGAM GENE, on one or more VGAM323 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4485] It is yet further appreciated that a function of VGAM323 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM323 include diagnosis, prevention and

treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM323 correlate with, and may be deduced from, the identity of the host target genes which VGAM323 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4486] Nucleotide sequences of the VGAM323 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM323 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM323 are further described hereinbelow with reference to Table 1.

[4487] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM323 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4488] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 324 (VGAM324) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4489] VGAM324 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM324 was detected is described hereinabove with reference to Figs. 2–8.

[4490] VGAM324 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4491] VGAM324 gene, herein designated VGAM GENE, encodes a VGAM324 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM324 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM324 precursor RNA is designated SEQ ID:8319, and is provided hereinbelow with reference to the sequence listing part.

[4492] VGAM324 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM324 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4493] An enzyme complex designated DICER COMPLEX, dices the VGAM324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM324 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM324 RNA is designated SEQ ID:8320, and is provided hereinbelow with reference to the sequence listing part.

[4494] VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM324 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4495] VGAM324 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM324 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM324 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4496] The complementary binding of VGAM324 RNA, herein designated VGAM RNA, to host target binding sites on VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM324 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4497] It is appreciated that VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM324 host target genes. The mRNA of each one of this plurality of VGAM324 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM324 RNA, herein designated VGAM RNA, and which when bound by VGAM324 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM324 host target proteins.

[4498] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM324 gene, herein designated VGAM GENE, on one or more VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4499] It is yet further appreciated that a function of VGAM324 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM324 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Spe-

cific functions, and accordingly utilities, of VGAM324 correlate with, and may be deduced from, the identity of the host target genes which VGAM324 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4500] Nucleotide sequences of the VGAM324 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM324 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM324 are further described hereinbelow with reference to Table 1.

[4501] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM324 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4502] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 325 (VGAM325) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[4503] VGAM325 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM325 was detected is described hereinabove with reference to Figs. 2–8.

[4504] VGAM325 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4505] VGAM325 gene, herein designated VGAM GENE, encodes a VGAM325 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM325 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM325 precursor RNA is designated SEQ ID:8331, and is provided hereinbelow with reference to the sequence listing part.

[4506] VGAM325 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM325 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4507] An enzyme complex designated DICER COMPLEX, dices the VGAM325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM325 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM325 RNA is designated SEQ ID:8332, and is provided hereinbelow with reference to the sequence listing part.

[4508] VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM325 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4509] VGAM325 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM325 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM325 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4510] The complementary binding of VGAM325 RNA, herein designated VGAM RNA, to host target binding sites on VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM325 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4511] It is appreciated that VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM325 host target genes. The mRNA of each one of this plurality of VGAM325 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM325 RNA, herein designated VGAM RNA, and which when bound by VGAM325 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM325 host target proteins.

[4512] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM325 gene, herein designated VGAM GENE, on one or more VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4513] It is yet further appreciated that a function of VGAM325 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM325 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM325 cor-



relate with, and may be deduced from, the identity of the host target genes which VGAM325 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4514] Nucleotide sequences of the VGAM325 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM325 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM325 are further described hereinbelow with reference to Table 1.

[4515] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM325 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4516] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 326 (VGAM326) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

- [4517] VGAM326 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM326 was detected is described hereinabove with reference to Figs. 2–8.
- [4518] VGAM326 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lactate dehydrogenase–elevating virus. VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [4519] VGAM326 gene, herein designated VGAM GENE, encodes a VGAM326 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM326 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM326 precursor RNA is designated SEQ ID:8379, and is provided hereinbelow with reference to the sequence listing part.
- [4520] VGAM326 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4521] An enzyme complex designated DICER COMPLEX, dices the VGAM326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM326 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM326 RNA is designated SEQ ID:8380, and is provided hereinbelow with reference to the sequence listing part.

[4522] VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4523] VGAM326 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM326 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4524] The complementary binding of VGAM326 RNA, herein designated VGAM RNA, to host target binding sites on VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM326 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4525] It is appreciated that VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM326 host target genes. The mRNA of each one of this plurality of VGAM326 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM326 RNA, herein designated VGAM RNA, and which when bound by VGAM326 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM326 host target proteins.

[4526] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM326 gene, herein designated VGAM GENE, on one or more VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4527] It is yet further appreciated that a function of VGAM326 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of viral infection by Lactate dehydrogenase-elevating virus. Specific functions, and accordingly utilities, of VGAM326 correlate with, and may be deduced from, the

identity of the host target genes which VGAM326 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4528] Nucleotide sequences of the VGAM326 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM326 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM326 are further described hereinbelow with reference to Table 1.

[4529] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM326 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4530] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 327 (VGAM327) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4531] VGAM327 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM327 was detected is described hereinabove with reference to Figs. 2–8.

[4532] VGAM327 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM327 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4533] VGAM327 gene, herein designated VGAM GENE, encodes a VGAM327 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM327 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM327 precursor RNA is designated SEQ ID:8391, and is provided hereinbelow with reference to the sequence listing part.

[4534] VGAM327 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4535] An enzyme complex designated DICER COMPLEX, dices the VGAM327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM327 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM327 RNA is designated SEQ ID:8392, and is provided hereinbelow with reference to the sequence listing part.

[4536] VGAM327 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4537] VGAM327 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM327 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM327 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4538] The complementary binding of VGAM327 RNA, herein designated VGAM RNA, to host target binding sites on VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM327 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4539] It is appreciated that VGAM327 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM327 host target genes. The mRNA of each one of this plurality of VGAM327 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM327 RNA, herein designated VGAM RNA, and which when bound by VGAM327 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM327 host target proteins.

[4540] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM327 gene, herein designated VGAM GENE, on one or more VGAM327 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4541] It is yet further appreciated that a function of VGAM327 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM327 correlate with, and may be deduced from, the identity of the host target genes which VGAM327 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[4542] Nucleotide sequences of the VGAM327 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM327 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM327 are further described hereinbelow with reference to Table 1.

[4543] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM327 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4544] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 328 (VGAM328) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4545] VGAM328 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM328 was detected is described hereinabove with reference to Figs. 2–8.

[4546] VGAM328 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox virus.

VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4547] VGAM328 gene, herein designated VGAM GENE, encodes a VGAM328 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM328 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM328 precursor RNA is designated SEQ ID:8403, and is provided hereinbelow with reference to the sequence listing part.

[4548] VGAM328 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4549] An enzyme complex designated DICER COMPLEX, dices the VGAM328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM328 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM328 RNA is designated SEQ ID:8404, and is provided hereinbelow with reference to the sequence listing part.

[4550] VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4551] VGAM328 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM328 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[4552] The complementary binding of VGAM328 RNA, herein designated VGAM RNA, to host target binding sites on VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM328 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4553] It is appreciated that VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM328 host target genes. The mRNA of each one of this plurality of VGAM328 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM328 RNA, herein designated VGAM RNA, and which when bound by VGAM328 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM328 host target proteins.

[4554] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM328 gene, herein designated VGAM GENE, on one or more VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4555] It is yet further appreciated that a function of VGAM328 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of viral infection by Monkeypox virus. Specific functions, and accordingly utilities, of VGAM328 correlate with, and may be deduced from, the identity of the host target genes which VGAM328 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[4556] Nucleotide sequences of the VGAM328 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM328 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM328 are further described hereinbelow with reference to Table 1.

[4557] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM328 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4558] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 329 (VGAM329) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4559] VGAM329 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM329 was detected is described hereinabove with reference to Figs. 2–8.

[4560] VGAM329 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM329 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4561] VGAM329 gene, herein designated VGAM GENE, encodes a VGAM329 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM329 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM329 precursor RNA is designated SEQ ID:8410, and is provided hereinbelow with reference to the sequence listing part.

[4562] VGAM329 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4563] An enzyme complex designated DICER COMPLEX, dices the VGAM329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM329 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM329 RNA is designated SEQ ID:8411, and is provided hereinbelow with reference to the sequence listing part.

[4564] VGAM329 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[4565] VGAM329 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM329 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4566] The complementary binding of VGAM329 RNA, herein designated VGAM RNA, to host target binding sites on VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM329 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4567] It is appreciated that VGAM329 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM329 host target genes. The mRNA of each one of this plurality of VGAM329 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM329 RNA, herein designated VGAM RNA, and which when bound by VGAM329 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM329 host target proteins.

[4568] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM329 gene, herein designated VGAM GENE, on one or

more VGAM329 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4569] It is yet further appreciated that a function of VGAM329 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM329 correlate with, and may be deduced from, the identity of the host target genes which VGAM329 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[4570] Nucleotide sequences of the VGAM329 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM329 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM329 are further described hereinbelow with reference to Table 1.

[4571] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM329 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4572] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 330 (VGAM330) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4573] VGAM330 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM330 was detected is described

hereinabove with reference to Figs. 2–8.

[4574] VGAM330 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM330 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4575] VGAM330 gene, herein designated VGAM GENE, encodes a VGAM330 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM330 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM330 precursor RNA is designated SEQ ID:8415, and is provided hereinbelow with reference to the sequence listing part.

[4576] VGAM330 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4577] An enzyme complex designated DICER COMPLEX, dices the VGAM330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM330 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM330 RNA is designated SEQ ID:8416, and is provided hereinbelow with reference to the sequence listing part.

[4578] VGAM330 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4579] VGAM330 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM330 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4580] The complementary binding of VGAM330 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM330 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4581] It is appreciated that VGAM330 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM330 host target genes. The mRNA of each one of this plurality of VGAM330 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM330 RNA, herein designated VGAM RNA, and which when bound by VGAM330 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM330 host target proteins.

[4582] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM330 gene, herein designated VGAM GENE, on one or more VGAM330 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4583] It is yet further appreciated that a function of VGAM330 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM330 correlate with, and may be deduced from, the identity of the host target genes which VGAM330 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4584] Nucleotide sequences of the VGAM330 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM330 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM330 are further described hereinbelow with reference to Table 1.

[4585] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM330 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4586] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 331 (VGAM331) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4587] VGAM331 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM331 was detected is described hereinabove with reference to Figs. 2-8.

[4588] VGAM331 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4589] VGAM331 gene, herein designated VGAM GENE, encodes a VGAM331 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM331 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM331 precursor RNA is designated SEQ ID:8422, and is provided hereinbelow with reference to the sequence listing part.

[4590] VGAM331 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[4591] An enzyme complex designated DICER COMPLEX, dices the VGAM331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM331 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM331 RNA is designated SEQ ID:8423, and is provided hereinbelow with reference to the sequence listing part.

[4592] VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4593] VGAM331 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM331 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4594] The complementary binding of VGAM331 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM331 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4595] It is appreciated that VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM331 host target genes. The mRNA of each one of this plurality of VGAM331 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM331 RNA, herein designated VGAM RNA, and which when bound by VGAM331 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM331 host target proteins.

[4596] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM331 gene, herein designated VGAM GENE, on one or more VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4597] It is yet further appreciated that a function of VGAM331 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM331 correlate with, and may be deduced from, the identity of the host target genes which VGAM331 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4598] Nucleotide sequences of the VGAM331 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM331 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM331 are further described hereinbelow with reference to Table 1.

[4599] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM331 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4600] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 332 (VGAM332) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4601] VGAM332 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM332 was detected is described hereinabove with reference to Figs. 2-8.

[4602] VGAM332 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine herpesvirus 2. VGAM332 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4603] VGAM332 gene, herein designated VGAM GENE, encodes a VGAM332 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM332 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM332 precursor RNA is designated SEQ ID:8426, and is provided hereinbelow with reference to the sequence listing part.

[4604] VGAM332 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4605] An enzyme complex designated DICER COMPLEX, dices the VGAM332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM332 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM332 RNA is designated SEQ ID:8427, and is provided hereinbelow with reference to the sequence listing part.

[4606] VGAM332 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4607] VGAM332 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM332 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM332 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4608] The complementary binding of VGAM332 RNA, herein designated VGAM RNA, to host target binding sites on VGAM332 host target RNA, herein designated VGAM HOST



TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM332 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4609] It is appreciated that VGAM332 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM332 host target genes. The mRNA of each one of this plurality of VGAM332 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM332 RNA, herein designated VGAM RNA, and which when bound by VGAM332 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM332 host target proteins.

[4610] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM332 gene, herein designated VGAM GENE, on one or more VGAM332 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4611] It is yet further appreciated that a function of VGAM332 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM332 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM332 correlate with, and may be deduced from, the identity of the host target genes which VGAM332 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4612] Nucleotide sequences of the VGAM332 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM332 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM332 are further described hereinbelow with reference to Table 1.

[4613] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM332 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4614] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 333 (VGAM333) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4615] VGAM333 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM333 was detected is described hereinabove with reference to Figs. 2-8.

[4616] VGAM333 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus.

VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4617] VGAM333 gene, herein designated VGAM GENE, encodes a VGAM333 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM333 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM333 precursor RNA is designated SEQ ID:8466, and is provided hereinbelow with reference to the sequence listing part.

[4618] VGAM333 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4619] An enzyme complex designated DICER COMPLEX, dices

the VGAM333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM333 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM333 RNA is designated SEQ ID:8467, and is provided hereinbelow with reference to the sequence listing part.

[4620] VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4621] VGAM333 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM333 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM333 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM333 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4622] The complementary binding of VGAM333 RNA, herein designated VGAM RNA, to host target binding sites on VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM333 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4623] It is appreciated that VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM333 host target genes. The mRNA of each one of this plurality of VGAM333 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM333 RNA, herein designated VGAM RNA, and which when bound by VGAM333 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM333 host target proteins.

[4624] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM333 gene, herein designated VGAM GENE, on one or more VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4625] It is yet further appreciated that a function of VGAM333 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM333 correlate with, and may be deduced from, the identity of the host target genes which VGAM333 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4626] Nucleotide sequences of the VGAM333 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM333 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM333 are further described hereinbelow with reference to Table 1.

[4627] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM333 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4628] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 334 (VGAM334) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4629] VGAM334 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM334 was detected is described hereinabove with reference to Figs. 2-8.

[4630] VGAM334 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM334 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[4631] VGAM334 gene, herein designated VGAM GENE, encodes a VGAM334 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM334 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM334 precursor RNA is designated SEQ ID:8475, and is provided hereinbelow with reference to the sequence listing part.

[4632] VGAM334 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4633] An enzyme complex designated DICER COMPLEX, dices the VGAM334 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM334 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM334 RNA is designated SEQ ID:8476, and is provided hereinbelow with reference to the sequence listing part.

[4634] VGAM334 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4635] VGAM334 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM334 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM334 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4636] The complementary binding of VGAM334 RNA, herein designated VGAM RNA, to host target binding sites on VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM334 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM334 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4637] It is appreciated that VGAM334 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM334 host target genes. The mRNA of each one of this plurality of VGAM334 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM334 RNA, herein designated VGAM RNA, and which when bound by VGAM334 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM334 host target proteins.

[4638] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM334 gene, herein designated VGAM GENE, on one or more VGAM334 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4639] It is yet further appreciated that a function of VGAM334 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM334 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM334 correlate with, and may be deduced from, the identity of the host target genes which VGAM334 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4640] Nucleotide sequences of the VGAM334 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM334 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM334 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM334 are further described hereinbelow with reference to Table 1.

[4641] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM334 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4642] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 335 (VGAM335) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4643] VGAM335 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM335 was detected is described hereinabove with reference to Figs. 2-8.

[4644] VGAM335 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[4645] VGAM335 gene, herein designated VGAM GENE, encodes a VGAM335 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM335 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM335 precursor RNA is designated SEQ ID:8521, and is provided hereinbelow with reference to the sequence listing part.

[4646] VGAM335 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4647] An enzyme complex designated DICER COMPLEX, dices the VGAM335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM335 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM335 RNA is designated SEQ ID:8522, and is provided hereinbelow with reference to the sequence listing part.

[4648] VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4649] VGAM335 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM335 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM335 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4650] The complementary binding of VGAM335 RNA, herein designated VGAM RNA, to host target binding sites on VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM335 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4651] It is appreciated that VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM335 host target genes. The mRNA of each one of this plurality of VGAM335 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM335 RNA, herein designated VGAM RNA, and which when bound by VGAM335 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM335 host target proteins.

[4652] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM335 gene, herein designated VGAM GENE, on one or more VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4653] It is yet further appreciated that a function of VGAM335 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM335 correlate with, and may be deduced from, the identity of the host target genes which VGAM335 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4654] Nucleotide sequences of the VGAM335 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM335 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM335 are further de-

scribed hereinbelow with reference to Table 1.

[4655] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM335 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4656] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 336 (VGAM336) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4657] VGAM336 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM336 was detected is described hereinabove with reference to Figs. 2-8.

[4658] VGAM336 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4659] VGAM336 gene, herein designated VGAM GENE, encodes a VGAM336 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM336 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM336 precursor RNA is designated SEQ ID:8529, and is provided hereinbelow with reference to the sequence listing part.

[4660] VGAM336 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4661] An enzyme complex designated DICER COMPLEX, dices the VGAM336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM336 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM336 RNA is designated SEQ ID:8530, and is provided hereinbelow with reference to the sequence listing part.

[4662] VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4663] VGAM336 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM336 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM336 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4664] The complementary binding of VGAM336 RNA, herein designated VGAM RNA, to host target binding sites on VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM336 host target protein, herein designated



VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4665] It is appreciated that VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM336 host target genes. The mRNA of each one of this plurality of VGAM336 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM336 RNA, herein designated VGAM RNA, and which when bound by VGAM336 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM336 host target proteins.

[4666] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM336 gene, herein designated VGAM GENE, on one or more VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4667] It is yet further appreciated that a function of VGAM336 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM336 correlate with, and may be deduced from, the identity of the host target genes which VGAM336 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4668] Nucleotide sequences of the VGAM336 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM336 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM336 are further described hereinbelow with reference to Table 1.

[4669] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM336 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4670] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 337 (VGAM337) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4671] VGAM337 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM337 was detected is described hereinabove with reference to Figs. 2-8.

[4672] VGAM337 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4673] VGAM337 gene, herein designated VGAM GENE, encodes a

VGAM337 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM337 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM337 precursor RNA is designated SEQ ID:8550, and is provided hereinbelow with reference to the sequence listing part.

[4674] VGAM337 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4675] An enzyme complex designated DICER COMPLEX, dices the VGAM337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM337 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM337 RNA is designated SEQ ID:8551, and is provided hereinbelow with reference to the sequence listing part.

[4676] VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4677] VGAM337 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM337 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4678] The complementary binding of VGAM337 RNA, herein designated VGAM RNA, to host target binding sites on VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM337 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[4679] It is appreciated that VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM337 host target genes. The mRNA of each one of this plurality of VGAM337 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM337 RNA, herein designated VGAM RNA, and which when bound by VGAM337 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM337 host target proteins.

[4680] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM337 gene, herein designated VGAM GENE, on one or more VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4681] It is yet further appreciated that a function of VGAM337 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM337 correlate with, and may be deduced from, the identity of the host target genes which VGAM337 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4682] Nucleotide sequences of the VGAM337 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM337 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM337 are further described hereinbelow with reference to Table 1.

[4683] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM337 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4684] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 338 (VGAM338) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4685] VGAM338 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM338 was detected is described hereinabove with reference to Figs. 2-8.

[4686] VGAM338 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4687] VGAM338 gene, herein designated VGAM GENE, encodes a VGAM338 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM338 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM338 precursor RNA is designated SEQ ID:8668, and is provided hereinbelow with reference to the sequence listing part.

[4688] VGAM338 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4689] An enzyme complex designated DICER COMPLEX, dices the VGAM338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM338 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM338 RNA is designated SEQ ID:8669, and is provided hereinbelow with reference to the sequence listing part.

[4690] VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4691] VGAM338 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM338 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM338 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4692] The complementary binding of VGAM338 RNA, herein designated VGAM RNA, to host target binding sites on VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM338 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4693] It is appreciated that VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM338 host target genes. The mRNA of each one of this plurality of VGAM338 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM338 RNA, herein designated VGAM RNA, and which when bound by VGAM338 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM338 host target proteins.

[4694] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM338 gene, herein designated VGAM GENE, on one or more VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4695] It is yet further appreciated that a function of VGAM338 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM338 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM338 correlate with, and may be deduced from, the identity of the host target genes which VGAM338 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4696] Nucleotide sequences of the VGAM338 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM338 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM338 are further described hereinbelow with reference to Table 1.

[4697] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM338 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4698] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 339 (VGAM339) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4699] VGAM339 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM339 was detected is described hereinabove with reference to Figs. 2–8.

[4700] VGAM339 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM339 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4701] VGAM339 gene, herein designated VGAM GENE, encodes a VGAM339 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM339 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM339 precursor RNA is designated SEQ ID:8675, and is provided hereinbelow with reference to the sequence listing part.

[4702] VGAM339 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4703] An enzyme complex designated DICER COMPLEX, dices the VGAM339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM339 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM339 RNA is designated SEQ ID:8676, and is provided hereinbelow with reference to the sequence listing part.

[4704] VGAM339 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4705] VGAM339 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM339 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM339 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4706] The complementary binding of VGAM339 RNA, herein designated VGAM RNA, to host target binding sites on VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM339 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4707] It is appreciated that VGAM339 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM339 host target genes. The mRNA of each one of this plurality of VGAM339 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM339 RNA, herein designated VGAM RNA, and which when bound by VGAM339 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM339 host target proteins.

[4708] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM339 gene, herein designated VGAM GENE, on one or more VGAM339 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4709] It is yet further appreciated that a function of VGAM339 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM339 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM339 correlate with, and may be deduced from, the identity of the host target genes which VGAM339 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4710] Nucleotide sequences of the VGAM339 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM339 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM339 are further described hereinbelow with reference to Table 1.

[4711] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM339 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4712] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 340 (VGAM340) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4713] VGAM340 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM340 was detected is described hereinabove with reference to Figs. 2–8.

[4714] VGAM340 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4715] VGAM340 gene, herein designated VGAM GENE, encodes a VGAM340 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM340 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM340 precursor RNA is designated SEQ ID:8680, and is provided hereinbelow with reference to the sequence listing part.

[4716] VGAM340 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4717] An enzyme complex designated DICER COMPLEX, dices the VGAM340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM340 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 55%) nucleotide sequence of VGAM340 RNA is designated SEQ ID:8681, and is provided hereinbelow with reference to the sequence listing part.

[4718] VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4719] VGAM340 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM340 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4720] The complementary binding of VGAM340 RNA, herein designated VGAM RNA, to host target binding sites on VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM340 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4721] It is appreciated that VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM340 host target genes. The mRNA of each one of this plurality of VGAM340 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM340 RNA, herein designated VGAM RNA, and which when bound by VGAM340 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM340 host target proteins.

[4722] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM340 gene, herein designated VGAM GENE, on one or more VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[4723] It is yet further appreciated that a function of VGAM340 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM340 correlate with, and may be deduced from, the identity of the host target genes which VGAM340 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4724] Nucleotide sequences of the VGAM340 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM340 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM340 are further described hereinbelow with reference to Table 1.

[4725] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM340 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4726] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 341 (VGAM341) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4727] VGAM341 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM341 was detected is described hereinabove with reference to Figs. 2–8.

[4728] VGAM341 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM341 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4729] VGAM341 gene, herein designated VGAM GENE, encodes a VGAM341 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM341 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM341 precursor RNA is designated SEQ ID:8691, and is provided hereinbelow with reference to the sequence listing part.

[4730] VGAM341 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4731] An enzyme complex designated DICER COMPLEX, dices the VGAM341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM341 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM341 RNA is designated SEQ ID:8692, and is provided hereinbelow with reference to the sequence listing part.

[4732] VGAM341 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM341 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM341 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4733] VGAM341 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM341 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM341 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM341 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM341 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4734] The complementary binding of VGAM341 RNA, herein designated VGAM RNA, to host target binding sites on VGAM341 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM341 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM341 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4735] It is appreciated that VGAM341 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM341 host target genes. The mRNA of

each one of this plurality of VGAM341 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM341 RNA, herein designated VGAM RNA, and which when bound by VGAM341 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM341 host target proteins.

[4736] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM341 gene, herein designated VGAM GENE, on one or more VGAM341 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[4737] It is yet further appreciated that a function of VGAM341 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM341 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM341 correlate with, and may be deduced from, the identity of the host target genes which VGAM341 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4738] Nucleotide sequences of the VGAM341 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM341 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM341 are further described hereinbelow with reference to Table 1.

[4739] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM341 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[4740] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 342 (VGAM342) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4741] VGAM342 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM342 was detected is described hereinabove with reference to Figs. 2–8.

[4742] VGAM342 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM342 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4743] VGAM342 gene, herein designated VGAM GENE, encodes a VGAM342 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM342 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM342 precursor RNA is designated SEQ ID:8724, and is provided hereinbelow with reference to the sequence listing part.

[4744] VGAM342 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM342 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4745] An enzyme complex designated DICER COMPLEX, dices the VGAM342 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM342 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM342 RNA is designated SEQ ID:8725, and

is provided hereinbelow with reference to the sequence listing part.

[4746] VGAM342 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM342 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM342 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4747] VGAM342 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM342 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM342 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM342 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM342 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4748] The complementary binding of VGAM342 RNA, herein designated VGAM RNA, to host target binding sites on VGAM342 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM342 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM342 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4749] It is appreciated that VGAM342 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM342 host target genes. The mRNA of each one of this plurality of VGAM342 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM342 RNA, herein designated VGAM RNA, and which when bound by VGAM342 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM342 host target proteins.

[4750] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM342 gene, herein designated VGAM GENE, on one or more VGAM342 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4751] It is yet further appreciated that a function of VGAM342 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM342 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM342 correlate with, and may be deduced from, the identity of the host target genes which VGAM342 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4752] Nucleotide sequences of the VGAM342 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM342 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM342 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM342 are further described hereinbelow with reference to Table 1.

[4753] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM342 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4754] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 343 (VGAM343) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4755] VGAM343 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM343 was detected is described hereinabove with reference to Figs. 2–8.

[4756] VGAM343 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Macaca mulatta* rhadinovirus. VGAM343 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4757] VGAM343 gene, herein designated VGAM GENE, encodes a VGAM343 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM343 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM343 precursor RNA is

designated SEQ ID:8752, and is provided hereinbelow with reference to the sequence listing part.

[4758] VGAM343 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM343 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4759] An enzyme complex designated DICER COMPLEX, dices the VGAM343 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM343 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM343 RNA is designated SEQ ID:8725, and is provided hereinbelow with reference to the sequence



listing part.

[4760] VGAM343 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM343 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM343 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4761] VGAM343 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM343 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM343 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM343 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM343 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4762] The complementary binding of VGAM343 RNA, herein designated VGAM RNA, to host target binding sites on VGAM343 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM343 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM343 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4763] It is appreciated that VGAM343 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM343 host target genes. The mRNA of each one of this plurality of VGAM343 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM343 RNA, herein designated VGAM RNA, and which when bound by VGAM343 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM343 host target proteins.

[4764] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM343 gene, herein designated VGAM GENE, on one or more VGAM343 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4765] It is yet further appreciated that a function of VGAM343 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM343 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM343 correlate with, and may be deduced from, the identity of the host target genes which VGAM343 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4766] Nucleotide sequences of the VGAM343 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM343 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM343 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM343 are further described hereinbelow with reference to Table 1.

[4767] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM343 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4768] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 344 (VGAM344) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4769] VGAM344 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM344 was detected is described hereinabove with reference to Figs. 2–8.

[4770] VGAM344 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM344 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4771] VGAM344 gene, herein designated VGAM GENE, encodes a VGAM344 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM344 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM344 precursor RNA is designated SEQ ID:8753, and is provided hereinbelow with

reference to the sequence listing part.

[4772] VGAM344 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4773] An enzyme complex designated DICER COMPLEX, dices the VGAM344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM344 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM344 RNA is designated SEQ ID:8754, and is provided hereinbelow with reference to the sequence listing part.

[4774] VGAM344 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM344 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM344 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4775] VGAM344 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM344 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM344 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM344 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM344 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4776] The complementary binding of VGAM344 RNA, herein designated VGAM RNA, to host target binding sites on VGAM344 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM344 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM344 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4777] It is appreciated that VGAM344 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM344 host target genes. The mRNA of each one of this plurality of VGAM344 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM344 RNA, herein designated VGAM RNA, and which when bound by VGAM344 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM344 host target proteins.

[4778] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM344 gene, herein designated VGAM GENE, on one or more VGAM344 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4779] It is yet further appreciated that a function of VGAM344 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM344 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM344 correlate with, and may be deduced from, the identity of the host target genes which VGAM344 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4780] Nucleotide sequences of the VGAM344 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM344 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM344 are further described hereinbelow with reference to Table 1.

[4781] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM344 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4782] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 345 (VGAM345) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4783] VGAM345 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM345 was detected is described hereinabove with reference to Figs. 2–8.

[4784] VGAM345 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM345 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4785] VGAM345 gene, herein designated VGAM GENE, encodes a VGAM345 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM345 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM345 precursor RNA is designated SEQ ID:8784, and is provided hereinbelow with reference to the sequence listing part.

[4786] VGAM345 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4787] An enzyme complex designated DICER COMPLEX, dices the VGAM345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM345 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM345 RNA is designated SEQ ID:8785, and is provided hereinbelow with reference to the sequence listing part.

[4788] VGAM345 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM345 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM345 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4789] VGAM345 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM345 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM345 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM345 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM345 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4790] The complementary binding of VGAM345 RNA, herein designated VGAM RNA, to host target binding sites on VGAM345 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM345 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM345 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4791] It is appreciated that VGAM345 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM345 host target genes. The mRNA of each one of this plurality of VGAM345 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM345 RNA, herein designated VGAM

RNA, and which when bound by VGAM345 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM345 host target proteins.

[4792] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM345 gene, herein designated VGAM GENE, on one or more VGAM345 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4793] It is yet further appreciated that a function of VGAM345 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM345 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM345 correlate with, and may be deduced from, the identity of the host target genes which VGAM345 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4794] Nucleotide sequences of the VGAM345 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM345 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM345 are further described hereinbelow with reference to Table 1.

[4795] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM345 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4796] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 346 (VGAM346) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4797] VGAM346 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM346 was detected is described hereinabove with reference to Figs. 2–8.

[4798] VGAM346 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM346 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4799] VGAM346 gene, herein designated VGAM GENE, encodes a VGAM346 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM346 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM346 precursor RNA is designated SEQ ID:8837, and is provided hereinbelow with reference to the sequence listing part.

[4800] VGAM346 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4801] An enzyme complex designated DICER COMPLEX, dices the VGAM346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM346 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM346 RNA is designated SEQ ID:8838, and is provided hereinbelow with reference to the sequence listing part.

[4802] VGAM346 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM346 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM346 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4803] VGAM346 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM346 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM346 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM346 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM346 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4804] The complementary binding of VGAM346 RNA, herein designated VGAM RNA, to host target binding sites on VGAM346 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM346 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM346 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4805] It is appreciated that VGAM346 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM346 host target genes. The mRNA of each one of this plurality of VGAM346 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM346 RNA, herein designated VGAM RNA, and which when bound by VGAM346 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM346 host target proteins.

[4806] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM346 gene, herein designated VGAM GENE, on one or more VGAM346 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4807] It is yet further appreciated that a function of VGAM346 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM346 include diagnosis, prevention and

treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM346 correlate with, and may be deduced from, the identity of the host target genes which VGAM346 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4808] Nucleotide sequences of the VGAM346 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM346 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM346 are further described hereinbelow with reference to Table 1.

[4809] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM346 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4810] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 347 (VGAM347) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4811] VGAM347 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM347 was detected is described hereinabove with reference to Figs. 2–8.

[4812] VGAM347 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM347 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4813] VGAM347 gene, herein designated VGAM GENE, encodes a VGAM347 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM347 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM347 precursor RNA is designated SEQ ID:8861, and is provided hereinbelow with reference to the sequence listing part.

[4814] VGAM347 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM347 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4815] An enzyme complex designated DICER COMPLEX, dices the VGAM347 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM347 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM347 RNA is designated SEQ ID:8862, and is provided hereinbelow with reference to the sequence listing part.

[4816] VGAM347 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM347 host target RNA, herein designated VGAM



HOST TARGET RNA. VGAM347 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4817] VGAM347 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM347 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM347 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM347 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM347 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4818] The complementary binding of VGAM347 RNA, herein designated VGAM RNA, to host target binding sites on VGAM347 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM347 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM347 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4819] It is appreciated that VGAM347 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM347 host target genes. The mRNA of each one of this plurality of VGAM347 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM347 RNA, herein designated VGAM RNA, and which when bound by VGAM347 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM347 host target proteins.

[4820] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM347 gene, herein designated VGAM GENE, on one or more VGAM347 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4821] It is yet further appreciated that a function of VGAM347 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM347 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Spe-

cific functions, and accordingly utilities, of VGAM347 correlate with, and may be deduced from, the identity of the host target genes which VGAM347 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4822] Nucleotide sequences of the VGAM347 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM347 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM347 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM347 are further described hereinbelow with reference to Table 1.

[4823] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM347 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4824] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 348 (VGAM348) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[4825] VGAM348 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM348 was detected is described hereinabove with reference to Figs. 2–8.

[4826] VGAM348 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM348 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4827] VGAM348 gene, herein designated VGAM GENE, encodes a VGAM348 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM348 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM348 precursor RNA is designated SEQ ID:8879, and is provided hereinbelow with reference to the sequence listing part.

[4828] VGAM348 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM348 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4829] An enzyme complex designated DICER COMPLEX, dices the VGAM348 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM348 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM348 RNA is designated SEQ ID:8880, and is provided hereinbelow with reference to the sequence listing part.

[4830] VGAM348 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM348 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM348 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4831] VGAM348 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM348 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM348 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM348 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM348 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4832] The complementary binding of VGAM348 RNA, herein designated VGAM RNA, to host target binding sites on VGAM348 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM348 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM348 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4833] It is appreciated that VGAM348 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM348 host target genes. The mRNA of each one of this plurality of VGAM348 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM348 RNA, herein designated VGAM RNA, and which when bound by VGAM348 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM348 host target proteins.



[4834] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM348 gene, herein designated VGAM GENE, on one or more VGAM348 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4835] It is yet further appreciated that a function of VGAM348 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM348 include diagnosis, prevention and treatment of viral infection by Macaca mulatta rhadinovirus. Specific functions, and accordingly utilities, of

VGAM348 correlate with, and may be deduced from, the identity of the host target genes which VGAM348 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4836] Nucleotide sequences of the VGAM348 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM348 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM348 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM348 are further described hereinbelow with reference to Table 1.

[4837] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM348 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4838] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 349 (VGAM349) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[4839] VGAM349 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM349 was detected is described hereinabove with reference to Figs. 2–8.

[4840] VGAM349 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM349 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4841] VGAM349 gene, herein designated VGAM GENE, encodes a VGAM349 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM349 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM349 precursor RNA is designated SEQ ID:8930, and is provided hereinbelow with reference to the sequence listing part.

[4842] VGAM349 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4843] An enzyme complex designated DICER COMPLEX, dices the VGAM349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM349 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM349 RNA is designated SEQ ID:8931, and is provided hereinbelow with reference to the sequence listing part.

[4844] VGAM349 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM349 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM349 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4845] VGAM349 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM349 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM349 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM349 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM349 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4846] The complementary binding of VGAM349 RNA, herein designated VGAM RNA, to host target binding sites on VGAM349 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM349 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM349 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4847] It is appreciated that VGAM349 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM349 host target genes. The mRNA of each one of this plurality of VGAM349 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM349 RNA, herein designated VGAM RNA, and which when bound by VGAM349 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM349 host target proteins.

[4848] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM349 gene, herein designated VGAM GENE, on one or more VGAM349 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4849] It is yet further appreciated that a function of VGAM349 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM349 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM349 correlate with, and may be deduced from, the identity of the

host target genes which VGAM349 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4850] Nucleotide sequences of the VGAM349 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM349 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM349 are further described hereinbelow with reference to Table 1.

[4851] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM349 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4852] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 350 (VGAM350) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[4853] VGAM350 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM350 was detected is described hereinabove with reference to Figs. 2–8.

[4854] VGAM350 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM350 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4855] VGAM350 gene, herein designated VGAM GENE, encodes a VGAM350 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM350 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM350 precursor RNA is designated SEQ ID:8958, and is provided hereinbelow with reference to the sequence listing part.

[4856] VGAM350 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4857] An enzyme complex designated DICER COMPLEX, dices the VGAM350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM350 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM350 RNA is designated SEQ ID:8959, and is provided hereinbelow with reference to the sequence listing part.

[4858] VGAM350 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM350 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM350 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4859] VGAM350 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM350 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM350 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM350 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM350 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4860] The complementary binding of VGAM350 RNA, herein designated VGAM RNA, to host target binding sites on VGAM350 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM350 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM350 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4861] It is appreciated that VGAM350 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM350 host target genes. The mRNA of each one of this plurality of VGAM350 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM350 RNA, herein designated VGAM RNA, and which when bound by VGAM350 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM350 host target proteins.

[4862] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM350 gene, herein designated VGAM GENE, on one or more VGAM350 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4863] It is yet further appreciated that a function of VGAM350 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM350 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM350 correlate with, and may be deduced from, the identity of the host target genes which VGAM350 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4864] Nucleotide sequences of the VGAM350 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM350 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM350 are further described hereinbelow with reference to Table 1.

[4865] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM350 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4866] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 351 (VGAM351) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4867] VGAM351 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM351 was detected is described hereinabove with reference to Figs. 2–8.

[4868] VGAM351 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM351 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4869] VGAM351 gene, herein designated VGAM GENE, encodes a VGAM351 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM351 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM351 precursor RNA is designated SEQ ID:8989, and is provided hereinbelow with reference to the sequence listing part.

[4870] VGAM351 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM351 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4871] An enzyme complex designated DICER COMPLEX, dices the VGAM351 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM351 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM351 RNA is designated SEQ ID:8990, and is provided hereinbelow with reference to the sequence listing part.

[4872] VGAM351 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM351 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM351 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4873] VGAM351 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM351 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM351 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM351 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM351 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[4874] The complementary binding of VGAM351 RNA, herein designated VGAM RNA, to host target binding sites on VGAM351 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM351 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM351 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4875] It is appreciated that VGAM351 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM351 host target genes. The mRNA of each one of this plurality of VGAM351 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM351 RNA, herein designated VGAM RNA, and which when bound by VGAM351 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM351 host target proteins.

[4876] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM351 gene, herein designated VGAM GENE, on one or more VGAM351 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4877] It is yet further appreciated that a function of VGAM351 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM351 include diagnosis, prevention and treatment of viral infection by Macaca mulatta rhadinovirus. Specific functions, and accordingly utilities, of VGAM351 correlate with, and may be deduced from, the identity of the host target genes which VGAM351 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[4878] Nucleotide sequences of the VGAM351 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM351 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM351 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM351 are further described hereinbelow with reference to Table 1.

[4879] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM351 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4880] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 352 (VGAM352) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4881] VGAM352 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM352 was detected is described hereinabove with reference to Figs. 2–8.

[4882] VGAM352 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Macaca mulatta* rhadinovirus. VGAM352 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4883] VGAM352 gene, herein designated VGAM GENE, encodes a VGAM352 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM352 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM352 precursor RNA is designated SEQ ID:9006, and is provided hereinbelow with reference to the sequence listing part.

[4884] VGAM352 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM352 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4885] An enzyme complex designated DICER COMPLEX, dices the VGAM352 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM352 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM352 RNA is designated SEQ ID:9007, and is provided hereinbelow with reference to the sequence listing part.

[4886] VGAM352 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM352 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM352 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[4887] VGAM352 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM352 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM352 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM352 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM352 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4888] The complementary binding of VGAM352 RNA, herein designated VGAM RNA, to host target binding sites on VGAM352 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM352 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM352 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4889] It is appreciated that VGAM352 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM352 host target genes. The mRNA of each one of this plurality of VGAM352 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM352 RNA, herein designated VGAM RNA, and which when bound by VGAM352 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM352 host target proteins.

[4890] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM352 gene, herein designated VGAM GENE, on one or



more VGAM352 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4891] It is yet further appreciated that a function of VGAM352 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM352 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM352 correlate with, and may be deduced from, the identity of the host target genes which VGAM352 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4892] Nucleotide sequences of the VGAM352 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM352 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM352 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM352 are further described hereinbelow with reference to Table 1.

[4893] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM352 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4894] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 353 (VGAM353) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4895] VGAM353 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM353 was detected is described

hereinabove with reference to Figs. 2–8.

[4896] VGAM353 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM353 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4897] VGAM353 gene, herein designated VGAM GENE, encodes a VGAM353 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM353 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM353 precursor RNA is designated SEQ ID:9013, and is provided hereinbelow with reference to the sequence listing part.

[4898] VGAM353 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4899] An enzyme complex designated DICER COMPLEX, dices the VGAM353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM353 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM353 RNA is designated SEQ ID:9014, and is provided hereinbelow with reference to the sequence listing part.

[4900] VGAM353 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM353 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM353 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4901] VGAM353 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM353 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM353 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM353 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM353 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4902] The complementary binding of VGAM353 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM353 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM353 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM353 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4903] It is appreciated that VGAM353 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM353 host target genes. The mRNA of each one of this plurality of VGAM353 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM353 RNA, herein designated VGAM RNA, and which when bound by VGAM353 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM353 host target proteins.

[4904] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM353 gene, herein designated VGAM GENE, on one or more VGAM353 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4905] It is yet further appreciated that a function of VGAM353 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM353 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM353 correlate with, and may be deduced from, the identity of the host target genes which VGAM353 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4906] Nucleotide sequences of the VGAM353 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM353 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM353 are further described hereinbelow with reference to Table 1.

[4907] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM353 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4908] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 354 (VGAM354) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4909] VGAM354 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM354 was detected is described hereinabove with reference to Figs. 2-8.



[4910] VGAM354 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM354 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4911] VGAM354 gene, herein designated VGAM GENE, encodes a VGAM354 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM354 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM354 precursor RNA is designated SEQ ID:9074, and is provided hereinbelow with reference to the sequence listing part.

[4912] VGAM354 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[4913] An enzyme complex designated DICER COMPLEX, dices the VGAM354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM354 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM354 RNA is designated SEQ ID:9075, and is provided hereinbelow with reference to the sequence listing part.

[4914] VGAM354 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM354 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM354 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4915] VGAM354 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM354 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM354 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM354 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM354 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4916] The complementary binding of VGAM354 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM354 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM354 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM354 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4917] It is appreciated that VGAM354 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM354 host target genes. The mRNA of each one of this plurality of VGAM354 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM354 RNA, herein designated VGAM RNA, and which when bound by VGAM354 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM354 host target proteins.

[4918] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM354 gene, herein designated VGAM GENE, on one or more VGAM354 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4919] It is yet further appreciated that a function of VGAM354 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM354 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM354 correlate with, and may be deduced from, the identity of the host target genes which VGAM354 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4920] Nucleotide sequences of the VGAM354 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM354 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM354 are further described hereinbelow with reference to Table 1.

[4921] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM354 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4922] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 355 (VGAM355) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4923] VGAM355 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM355 was detected is described hereinabove with reference to Figs. 2-8.

[4924] VGAM355 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Swinepox virus.

VGAM355 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4925] VGAM355 gene, herein designated VGAM GENE, encodes a VGAM355 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM355 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM355 precursor RNA is designated SEQ ID:9094, and is provided hereinbelow with reference to the sequence listing part.

[4926] VGAM355 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4927] An enzyme complex designated DICER COMPLEX, dices the VGAM355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM355 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM355 RNA is designated SEQ ID:9095, and is provided hereinbelow with reference to the sequence listing part.

[4928] VGAM355 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM355 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM355 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4929] VGAM355 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM355 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM355 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM355 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM355 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4930] The complementary binding of VGAM355 RNA, herein designated VGAM RNA, to host target binding sites on VGAM355 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM355 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM355 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4931] It is appreciated that VGAM355 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM355 host target genes. The mRNA of each one of this plurality of VGAM355 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM355 RNA, herein designated VGAM RNA, and which when bound by VGAM355 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM355 host target proteins.

[4932] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM355 gene, herein designated VGAM GENE, on one or more VGAM355 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4933] It is yet further appreciated that a function of VGAM355 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM355 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM355 correlate with, and may be deduced from, the identity of the host target genes which VGAM355 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4934] Nucleotide sequences of the VGAM355 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM355 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM355 are further described hereinbelow with reference to Table 1.

[4935] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM355 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4936] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 356 (VGAM356) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4937] VGAM356 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM356 was detected is described hereinabove with reference to Figs. 2-8.

[4938] VGAM356 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus.

VGAM356 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4939] VGAM356 gene, herein designated VGAM GENE, encodes a VGAM356 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM356 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM356 precursor RNA is designated SEQ ID:9102, and is provided hereinbelow with reference to the sequence listing part.

[4940] VGAM356 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM356 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4941] An enzyme complex designated DICER COMPLEX, dices

the VGAM356 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM356 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM356 RNA is designated SEQ ID:9103, and is provided hereinbelow with reference to the sequence listing part.

[4942] VGAM356 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM356 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM356 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4943] VGAM356 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM356 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM356 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM356 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM356 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4944] The complementary binding of VGAM356 RNA, herein designated VGAM RNA, to host target binding sites on VGAM356 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM356 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM356 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4945] It is appreciated that VGAM356 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM356 host target genes. The mRNA of each one of this plurality of VGAM356 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM356 RNA, herein designated VGAM RNA, and which when bound by VGAM356 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM356 host target proteins.

[4946] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM356 gene, herein designated VGAM GENE, on one or more VGAM356 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4947] It is yet further appreciated that a function of VGAM356 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM356 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM356 correlate with, and may be deduced from, the identity of the host target genes which VGAM356 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4948] Nucleotide sequences of the VGAM356 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM356 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM356 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM356 are further described hereinbelow with reference to Table 1.

[4949] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM356 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4950] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 357 (VGAM357) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4951] VGAM357 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM357 was detected is described hereinabove with reference to Figs. 2-8.

[4952] VGAM357 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM357 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[4953] VGAM357 gene, herein designated VGAM GENE, encodes a VGAM357 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM357 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM357 precursor RNA is designated SEQ ID:9143, and is provided hereinbelow with reference to the sequence listing part.

[4954] VGAM357 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM357 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4955] An enzyme complex designated DICER COMPLEX, dices the VGAM357 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM357 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM357 RNA is designated SEQ ID:9144, and is provided hereinbelow with reference to the sequence listing part.

[4956] VGAM357 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM357 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM357 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4957] VGAM357 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM357 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM357 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM357 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM357 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4958] The complementary binding of VGAM357 RNA, herein designated VGAM RNA, to host target binding sites on VGAM357 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM357 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM357 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4959] It is appreciated that VGAM357 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM357 host target genes. The mRNA of each one of this plurality of VGAM357 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM357 RNA, herein designated VGAM RNA, and which when bound by VGAM357 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM357 host target proteins.

[4960] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM357 gene, herein designated VGAM GENE, on one or more VGAM357 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4961] It is yet further appreciated that a function of VGAM357 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM357 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM357 correlate with, and may be deduced from, the identity of the host target genes which VGAM357 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4962] Nucleotide sequences of the VGAM357 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM357 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM357 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM357 are further described hereinbelow with reference to Table 1.

[4963] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM357 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4964] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 358 (VGAM358) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4965] VGAM358 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM358 was detected is described hereinabove with reference to Figs. 2-8.

[4966] VGAM358 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM358 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[4967] VGAM358 gene, herein designated VGAM GENE, encodes a VGAM358 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM358 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM358 precursor RNA is designated SEQ ID:9215, and is provided hereinbelow with reference to the sequence listing part.

[4968] VGAM358 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4969] An enzyme complex designated DICER COMPLEX, dices the VGAM358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM358 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM358 RNA is designated SEQ ID:9216, and is provided hereinbelow with reference to the sequence listing part.

[4970] VGAM358 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM358 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM358 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4971] VGAM358 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM358 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM358 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM358 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM358 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4972] The complementary binding of VGAM358 RNA, herein designated VGAM RNA, to host target binding sites on VGAM358 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM358 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM358 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4973] It is appreciated that VGAM358 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM358 host target genes. The mRNA of each one of this plurality of VGAM358 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM358 RNA, herein designated VGAM RNA, and which when bound by VGAM358 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM358 host target proteins.

[4974] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM358 gene, herein designated VGAM GENE, on one or more VGAM358 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4975] It is yet further appreciated that a function of VGAM358 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM358 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM358 correlate with, and may be deduced from, the identity of the host target genes which VGAM358 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4976] Nucleotide sequences of the VGAM358 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM358 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM358 are further de-

scribed hereinbelow with reference to Table 1.

[4977] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM358 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4978] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 359 (VGAM359) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4979] VGAM359 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM359 was detected is described hereinabove with reference to Figs. 2-8.

[4980] VGAM359 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM359 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4981] VGAM359 gene, herein designated VGAM GENE, encodes a VGAM359 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM359 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM359 precursor RNA is designated SEQ ID:9233, and is provided hereinbelow with reference to the sequence listing part.

[4982] VGAM359 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM359 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4983] An enzyme complex designated DICER COMPLEX, dices the VGAM359 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM359 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM359 RNA is designated SEQ ID:9234, and is provided hereinbelow with reference to the sequence listing part.

[4984] VGAM359 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM359 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM359 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4985] VGAM359 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM359 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM359 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM359 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM359 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[4986] The complementary binding of VGAM359 RNA, herein designated VGAM RNA, to host target binding sites on VGAM359 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM359 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM359 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[4987] It is appreciated that VGAM359 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM359 host target genes. The mRNA of each one of this plurality of VGAM359 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM359 RNA, herein designated VGAM RNA, and which when bound by VGAM359 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM359 host target proteins.

[4988] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM359 gene, herein designated VGAM GENE, on one or more VGAM359 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[4989] It is yet further appreciated that a function of VGAM359 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM359 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM359 correlate with, and may be deduced from, the identity of the host target genes which VGAM359 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[4990] Nucleotide sequences of the VGAM359 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM359 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM359 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM359 are further described hereinbelow with reference to Table 1.

[4991] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM359 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[4992] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 360 (VGAM360) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[4993] VGAM360 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM360 was detected is described hereinabove with reference to Figs. 2-8.

[4994] VGAM360 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM360 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[4995] VGAM360 gene, herein designated VGAM GENE, encodes a

VGAM360 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM360 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM360 precursor RNA is designated SEQ ID:9284, and is provided hereinbelow with reference to the sequence listing part.

[4996] VGAM360 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[4997] An enzyme complex designated DICER COMPLEX, dices the VGAM360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM360 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM360 RNA is designated SEQ ID:9285, and is provided hereinbelow with reference to the sequence listing part.

[4998] VGAM360 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM360 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM360 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[4999] VGAM360 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM360 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM360 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM360 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM360 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5000] The complementary binding of VGAM360 RNA, herein designated VGAM RNA, to host target binding sites on VGAM360 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM360 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM360 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[5001] It is appreciated that VGAM360 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM360 host target genes. The mRNA of each one of this plurality of VGAM360 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM360 RNA, herein designated VGAM RNA, and which when bound by VGAM360 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM360 host target proteins.

[5002] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM360 gene, herein designated VGAM GENE, on one or more VGAM360 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5003] It is yet further appreciated that a function of VGAM360 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM360 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM360 correlate with, and may be deduced from, the identity of the host target genes which VGAM360 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5004] Nucleotide sequences of the VGAM360 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM360 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM360 are further described hereinbelow with reference to Table 1.

[5005] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM360 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5006] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 361 (VGAM361) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5007] VGAM361 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM361 was detected is described hereinabove with reference to Figs. 2-8.

[5008] VGAM361 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM361 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5009] VGAM361 gene, herein designated VGAM GENE, encodes a VGAM361 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM361 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM361 precursor RNA is designated SEQ ID:9308, and is provided hereinbelow with reference to the sequence listing part.

[5010] VGAM361 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5011] An enzyme complex designated DICER COMPLEX, dices the VGAM361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM361 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM361 RNA is designated SEQ ID:9309, and is provided hereinbelow with reference to the sequence listing part.

[5012] VGAM361 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM361 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM361 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5013] VGAM361 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM361 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM361 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM361 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM361 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5014] The complementary binding of VGAM361 RNA, herein designated VGAM RNA, to host target binding sites on VGAM361 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM361 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM361 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5015] It is appreciated that VGAM361 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM361 host target genes. The mRNA of each one of this plurality of VGAM361 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM361 RNA, herein designated VGAM RNA, and which when bound by VGAM361 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM361 host target proteins.

[5016] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM361 gene, herein designated VGAM GENE, on one or more VGAM361 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5017] It is yet further appreciated that a function of VGAM361 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM361 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM361 correlate with, and may be deduced from, the identity of the host target genes which VGAM361 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5018] Nucleotide sequences of the VGAM361 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM361 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM361 are further described hereinbelow with reference to Table 1.

[5019] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM361 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5020] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 362 (VGAM362) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5021] VGAM362 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM362 was detected is described hereinabove with reference to Figs. 2–8.

[5022] VGAM362 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM362 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5023] VGAM362 gene, herein designated VGAM GENE, encodes a VGAM362 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike



most ordinary genes, VGAM362 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM362 precursor RNA is designated SEQ ID:9415, and is provided hereinbelow with reference to the sequence listing part.

[5024] VGAM362 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5025] An enzyme complex designated DICER COMPLEX, dices the VGAM362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM362 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM362 RNA is designated SEQ ID:9416, and is provided hereinbelow with reference to the sequence listing part.

[5026] VGAM362 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM362 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM362 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5027] VGAM362 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM362 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM362 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM362 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM362 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5028] The complementary binding of VGAM362 RNA, herein designated VGAM RNA, to host target binding sites on VGAM362 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM362 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM362 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5029] It is appreciated that VGAM362 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM362 host target genes. The mRNA of each one of this plurality of VGAM362 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM362 RNA, herein designated VGAM RNA, and which when bound by VGAM362 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM362 host target proteins.

[5030] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM362 gene, herein designated VGAM GENE, on one or more VGAM362 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5031] It is yet further appreciated that a function of VGAM362 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM362 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM362 correlate with, and may be deduced from, the identity of the host target genes which VGAM362 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5032] Nucleotide sequences of the VGAM362 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM362 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM362 are further described hereinbelow with reference to Table 1.

[5033] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM362 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5034] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 363 (VGAM363) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5035] VGAM363 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM363 was detected is described hereinabove with reference to Figs. 2–8.

[5036] VGAM363 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM363 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5037] VGAM363 gene, herein designated VGAM GENE, encodes a VGAM363 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM363 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM363 precursor RNA is designated SEQ ID:9471, and is provided hereinbelow with reference to the sequence listing part.

[5038] VGAM363 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5039] An enzyme complex designated DICER COMPLEX, dices the VGAM363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM363 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM363 RNA is designated SEQ ID:9472, and is provided hereinbelow with reference to the sequence listing part.

[5040] VGAM363 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM363 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM363 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5041] VGAM363 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM363 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM363 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM363 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM363 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5042] The complementary binding of VGAM363 RNA, herein designated VGAM RNA, to host target binding sites on VGAM363 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM363 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM363 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5043] It is appreciated that VGAM363 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM363 host target genes. The mRNA of each one of this plurality of VGAM363 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM363 RNA, herein designated VGAM RNA, and which when bound by VGAM363 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM363 host target proteins.

[5044] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM363 gene, herein designated VGAM GENE, on one or more VGAM363 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[5045] It is yet further appreciated that a function of VGAM363 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM363 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM363 correlate with, and may be deduced from, the identity of the host target genes which VGAM363 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5046] Nucleotide sequences of the VGAM363 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM363 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM363 are further described hereinbelow with reference to Table 1.

[5047] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM363 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5048] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 364 (VGAM364) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5049] VGAM364 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM364 was detected is described hereinabove with reference to Figs. 2–8.

[5050] VGAM364 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM364 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5051] VGAM364 gene, herein designated VGAM GENE, encodes a VGAM364 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM364 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM364 precursor RNA is designated SEQ ID:9478, and is provided hereinbelow with reference to the sequence listing part.

[5052] VGAM364 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5053] An enzyme complex designated DICER COMPLEX, dices the VGAM364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM364 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM364 RNA is designated SEQ ID:9479, and is provided hereinbelow with reference to the sequence listing part.

[5054] VGAM364 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM364 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM364 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5055] VGAM364 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM364 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM364 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM364 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM364 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5056] The complementary binding of VGAM364 RNA, herein designated VGAM RNA, to host target binding sites on VGAM364 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM364 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM364 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5057] It is appreciated that VGAM364 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM364 host target genes. The mRNA of

each one of this plurality of VGAM364 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM364 RNA, herein designated VGAM RNA, and which when bound by VGAM364 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM364 host target proteins.

[5058] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM364 gene, herein designated VGAM GENE, on one or more VGAM364 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[5059] It is yet further appreciated that a function of VGAM364 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM364 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM364 correlate with, and may be deduced from, the identity of the host target genes which VGAM364 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5060] Nucleotide sequences of the VGAM364 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM364 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM364 are further described hereinbelow with reference to Table 1.

[5061] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM364 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[5062] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 365 (VGAM365) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5063] VGAM365 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM365 was detected is described hereinabove with reference to Figs. 2–8.

[5064] VGAM365 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM365 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5065] VGAM365 gene, herein designated VGAM GENE, encodes a VGAM365 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM365 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM365 precursor RNA is designated SEQ ID:9488, and is provided hereinbelow with reference to the sequence listing part.

[5066] VGAM365 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM365 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5067] An enzyme complex designated DICER COMPLEX, dices the VGAM365 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM365 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM365 RNA is designated SEQ ID:9489, and

is provided hereinbelow with reference to the sequence listing part.

[5068] VGAM365 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM365 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM365 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5069] VGAM365 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM365 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM365 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM365 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM365 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5070] The complementary binding of VGAM365 RNA, herein designated VGAM RNA, to host target binding sites on VGAM365 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM365 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM365 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5071] It is appreciated that VGAM365 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM365 host target genes. The mRNA of each one of this plurality of VGAM365 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM365 RNA, herein designated VGAM RNA, and which when bound by VGAM365 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM365 host target proteins.

[5072] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM365 gene, herein designated VGAM GENE, on one or more VGAM365 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5073] It is yet further appreciated that a function of VGAM365 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM365 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM365 correlate with, and may be deduced from, the identity of the host target genes which VGAM365 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5074] Nucleotide sequences of the VGAM365 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM365 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM365 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM365 are further described hereinbelow with reference to Table 1.

[5075] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM365 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5076] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 366 (VGAM366) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5077] VGAM366 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM366 was detected is described hereinabove with reference to Figs. 2–8.

[5078] VGAM366 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM366 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5079] VGAM366 gene, herein designated VGAM GENE, encodes a VGAM366 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM366 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM366 precursor RNA is



designated SEQ ID:9497, and is provided hereinbelow with reference to the sequence listing part.

[5080] VGAM366 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM366 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5081] An enzyme complex designated DICER COMPLEX, dices the VGAM366 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM366 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM366 RNA is designated SEQ ID:9498, and is provided hereinbelow with reference to the sequence

listing part.

[5082] VGAM366 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM366 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM366 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5083] VGAM366 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM366 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM366 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM366 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM366 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5084] The complementary binding of VGAM366 RNA, herein designated VGAM RNA, to host target binding sites on VGAM366 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM366 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM366 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5085] It is appreciated that VGAM366 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM366 host target genes. The mRNA of each one of this plurality of VGAM366 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM366 RNA, herein designated VGAM RNA, and which when bound by VGAM366 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM366 host target proteins.

[5086] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM366 gene, herein designated VGAM GENE, on one or more VGAM366 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5087] It is yet further appreciated that a function of VGAM366 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM366 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM366 correlate with, and may be deduced from, the identity of the host target genes which VGAM366 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5088] Nucleotide sequences of the VGAM366 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM366 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM366 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM366 are further described hereinbelow with reference to Table 1.

[5089] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM366 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5090] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 367 (VGAM367) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5091] VGAM367 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM367 was detected is described hereinabove with reference to Figs. 2–8.

[5092] VGAM367 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM367 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5093] VGAM367 gene, herein designated VGAM GENE, encodes a VGAM367 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM367 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM367 precursor RNA is designated SEQ ID:9510, and is provided hereinbelow with

reference to the sequence listing part.

[5094] VGAM367 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5095] An enzyme complex designated DICER COMPLEX, dices the VGAM367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM367 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM367 RNA is designated SEQ ID:9511, and is provided hereinbelow with reference to the sequence listing part.

[5096] VGAM367 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM367 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM367 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5097] VGAM367 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM367 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM367 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM367 RNA, herein designated



VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM367 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5098] The complementary binding of VGAM367 RNA, herein designated VGAM RNA, to host target binding sites on VGAM367 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM367 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM367 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5099] It is appreciated that VGAM367 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM367 host target genes. The mRNA of each one of this plurality of VGAM367 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM367 RNA, herein designated VGAM RNA, and which when bound by VGAM367 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM367 host target proteins.

[5100] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM367 gene, herein designated VGAM GENE, on one or more VGAM367 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5101] It is yet further appreciated that a function of VGAM367 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM367 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM367 correlate with, and may be deduced from, the identity of the host target genes which VGAM367 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5102] Nucleotide sequences of the VGAM367 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM367 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM367 are further described hereinbelow with reference to Table 1.

[5103] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM367 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5104] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 368 (VGAM368) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5105] VGAM368 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM368 was detected is described hereinabove with reference to Figs. 2–8.

[5106] VGAM368 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM368 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5107] VGAM368 gene, herein designated VGAM GENE, encodes a VGAM368 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM368 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM368 precursor RNA is designated SEQ ID:9524, and is provided hereinbelow with reference to the sequence listing part.

[5108] VGAM368 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM368 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5109] An enzyme complex designated DICER COMPLEX, dices the VGAM368 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM368 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM368 RNA is designated SEQ ID:9525, and is provided hereinbelow with reference to the sequence listing part.

[5110] VGAM368 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM368 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM368 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5111] VGAM368 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM368 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM368 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM368 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM368 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5112] The complementary binding of VGAM368 RNA, herein designated VGAM RNA, to host target binding sites on VGAM368 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM368 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM368 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5113] It is appreciated that VGAM368 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM368 host target genes. The mRNA of each one of this plurality of VGAM368 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM368 RNA, herein designated VGAM

RNA, and which when bound by VGAM368 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM368 host target proteins.



[5114] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM368 gene, herein designated VGAM GENE, on one or more VGAM368 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5115] It is yet further appreciated that a function of VGAM368 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM368 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM368 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM368 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5116] Nucleotide sequences of the VGAM368 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM368 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM368 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM368 are further described hereinbelow with reference to Table 1.

[5117] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM368 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5118] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 369 (VGAM369) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[5119] VGAM369 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM369 was detected is described hereinabove with reference to Figs. 2–8.

[5120] VGAM369 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM369 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5121] VGAM369 gene, herein designated VGAM GENE, encodes a VGAM369 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM369 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM369 precursor RNA is designated SEQ ID:9531, and is provided hereinbelow with reference to the sequence listing part.

[5122] VGAM369 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM369 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5123] An enzyme complex designated DICER COMPLEX, dices the VGAM369 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM369 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM369 RNA is designated SEQ ID:9532, and is provided hereinbelow with reference to the sequence listing part.

[5124] VGAM369 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM369 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM369 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5125] VGAM369 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM369 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM369 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM369 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM369 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5126] The complementary binding of VGAM369 RNA, herein designated VGAM RNA, to host target binding sites on VGAM369 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM369 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM369 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5127] It is appreciated that VGAM369 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM369 host target genes. The mRNA of each one of this plurality of VGAM369 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM369 RNA, herein designated VGAM RNA, and which when bound by VGAM369 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM369 host target proteins.

[5128] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM369 gene, herein designated VGAM GENE, on one or more VGAM369 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5129] It is yet further appreciated that a function of VGAM369 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM369 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM369 correlate with, and may be deduced from, the identity of the

host target genes which VGAM369 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5130] Nucleotide sequences of the VGAM369 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM369 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM369 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM369 are further described hereinbelow with reference to Table 1.

[5131] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM369 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5132] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 370 (VGAM370) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[5133] VGAM370 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM370 was detected is described hereinabove with reference to Figs. 2–8.

[5134] VGAM370 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM370 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5135] VGAM370 gene, herein designated VGAM GENE, encodes a VGAM370 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM370 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM370 precursor RNA is designated SEQ ID:9561, and is provided hereinbelow with reference to the sequence listing part.

[5136] VGAM370 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5137] An enzyme complex designated DICER COMPLEX, dices the VGAM370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM370 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM370 RNA is designated SEQ ID:9562, and is provided hereinbelow with reference to the sequence listing part.

[5138] VGAM370 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM370 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM370 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5139] VGAM370 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM370 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM370 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM370 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM370 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5140] The complementary binding of VGAM370 RNA, herein designated VGAM RNA, to host target binding sites on VGAM370 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM370 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM370 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5141] It is appreciated that VGAM370 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM370 host target genes. The mRNA of each one of this plurality of VGAM370 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM370 RNA, herein designated VGAM RNA, and which when bound by VGAM370 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM370 host target proteins.

[5142] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM370 gene, herein designated VGAM GENE, on one or more VGAM370 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5143] It is yet further appreciated that a function of VGAM370 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM370 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM370 correlate with, and may be deduced from, the identity of the host target genes which VGAM370 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[5144] Nucleotide sequences of the VGAM370 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM370 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM370 are further described hereinbelow with reference to Table 1.

[5145] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM370 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5146] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 371 (VGAM371) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5147] VGAM371 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM371 was detected is described hereinabove with reference to Figs. 2–8.

[5148] VGAM371 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM371 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5149] VGAM371 gene, herein designated VGAM GENE, encodes a VGAM371 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM371 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM371 precursor RNA is designated SEQ ID:9641, and is provided hereinbelow with reference to the sequence listing part.

[5150] VGAM371 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5151] An enzyme complex designated DICER COMPLEX, dices the VGAM371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM371 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM371 RNA is designated SEQ ID:9642, and is provided hereinbelow with reference to the sequence listing part.

[5152] VGAM371 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM371 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM371 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5153] VGAM371 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM371 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM371 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM371 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM371 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[5154] The complementary binding of VGAM371 RNA, herein designated VGAM RNA, to host target binding sites on VGAM371 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM371 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM371 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5155] It is appreciated that VGAM371 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM371 host target genes. The mRNA of each one of this plurality of VGAM371 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM371 RNA, herein designated VGAM RNA, and which when bound by VGAM371 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM371 host target proteins.

[5156] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM371 gene, herein designated VGAM GENE, on one or more VGAM371 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5157] It is yet further appreciated that a function of VGAM371 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM371 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM371 correlate with, and may be deduced from, the identity of the host target genes which VGAM371 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[5158] Nucleotide sequences of the VGAM371 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM371 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM371 are further described hereinbelow with reference to Table 1.

[5159] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM371 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5160] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 372 (VGAM372) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5161] VGAM372 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM372 was detected is described hereinabove with reference to Figs. 2–8.

[5162] VGAM372 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM372 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5163] VGAM372 gene, herein designated VGAM GENE, encodes a VGAM372 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM372 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM372 precursor RNA is designated SEQ ID:9854, and is provided hereinbelow with reference to the sequence listing part.

[5164] VGAM372 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5165] An enzyme complex designated DICER COMPLEX, dices the VGAM372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM372 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM372 RNA is designated SEQ ID:9855, and is provided hereinbelow with reference to the sequence listing part.

[5166] VGAM372 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM372 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM372 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[5167] VGAM372 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM372 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM372 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM372 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM372 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5168] The complementary binding of VGAM372 RNA, herein designated VGAM RNA, to host target binding sites on VGAM372 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM372 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM372 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5169] It is appreciated that VGAM372 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM372 host target genes. The mRNA of each one of this plurality of VGAM372 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM372 RNA, herein designated VGAM RNA, and which when bound by VGAM372 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM372 host target proteins.

[5170] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM372 gene, herein designated VGAM GENE, on one or



more VGAM372 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5171] It is yet further appreciated that a function of VGAM372 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM372 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM372 correlate with, and may be deduced from, the identity of the host target genes which VGAM372 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5172] Nucleotide sequences of the VGAM372 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM372 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM372 are further described hereinbelow with reference to Table 1.

[5173] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM372 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5174] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 373 (VGAM373) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5175] VGAM373 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM373 was detected is described

hereinabove with reference to Figs. 2–8.

[5176] VGAM373 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8.

VGAM373 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5177] VGAM373 gene, herein designated VGAM GENE, encodes a VGAM373 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM373 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM373 precursor RNA is designated SEQ ID:9899, and is provided hereinbelow with reference to the sequence listing part.

[5178] VGAM373 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5179] An enzyme complex designated DICER COMPLEX, dices the VGAM373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM373 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM373 RNA is designated SEQ ID:9900, and is provided hereinbelow with reference to the sequence listing part.

[5180] VGAM373 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM373 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM373 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5181] VGAM373 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM373 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM373 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM373 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM373 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5182] The complementary binding of VGAM373 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM373 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM373 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM373 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5183] It is appreciated that VGAM373 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM373 host target genes. The mRNA of each one of this plurality of VGAM373 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM373 RNA, herein designated VGAM RNA, and which when bound by VGAM373 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM373 host target proteins.

[5184] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM373 gene, herein designated VGAM GENE, on one or more VGAM373 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5185] It is yet further appreciated that a function of VGAM373 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM373 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM373 correlate with, and may be deduced from, the identity of the host target genes which VGAM373 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5186] Nucleotide sequences of the VGAM373 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM373 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM373 are further described hereinbelow with reference to Table 1.

[5187] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM373 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5188] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 374 (VGAM374) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5189] VGAM374 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM374 was detected is described hereinabove with reference to Figs. 2-8.



[5190] VGAM374 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8.

VGAM374 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5191] VGAM374 gene, herein designated VGAM GENE, encodes a VGAM374 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM374 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM374 precursor RNA is designated SEQ ID:9925, and is provided hereinbelow with reference to the sequence listing part.

[5192] VGAM374 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[5193] An enzyme complex designated DICER COMPLEX, dices the VGAM374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM374 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM374 RNA is designated SEQ ID:9926, and is provided hereinbelow with reference to the sequence listing part.

[5194] VGAM374 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM374 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM374 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5195] VGAM374 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM374 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM374 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM374 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM374 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5196] The complementary binding of VGAM374 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM374 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM374 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM374 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5197] It is appreciated that VGAM374 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM374 host target genes. The mRNA of each one of this plurality of VGAM374 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM374 RNA, herein designated VGAM RNA, and which when bound by VGAM374 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM374 host target proteins.

[5198] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM374 gene, herein designated VGAM GENE, on one or more VGAM374 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5199] It is yet further appreciated that a function of VGAM374 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM374 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM374 correlate with, and may be deduced from, the identity of the host target genes which VGAM374 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5200] Nucleotide sequences of the VGAM374 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM374 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM374 are further described hereinbelow with reference to Table 1.

[5201] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM374 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5202] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 375 (VGAM375) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5203] VGAM375 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM375 was detected is described hereinabove with reference to Figs. 2-8.

[5204] VGAM375 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Bovine herpesvirus 1. VGAM375 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5205] VGAM375 gene, herein designated VGAM GENE, encodes a VGAM375 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM375 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM375 precursor RNA is designated SEQ ID:9929, and is provided hereinbelow with reference to the sequence listing part.

[5206] VGAM375 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM375 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5207] An enzyme complex designated DICER COMPLEX, dices the VGAM375 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM375 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM375 RNA is designated SEQ ID:9930, and is provided hereinbelow with reference to the sequence listing part.

[5208] VGAM375 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM375 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM375 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5209] VGAM375 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM375 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM375 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM375 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM375 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5210] The complementary binding of VGAM375 RNA, herein designated VGAM RNA, to host target binding sites on VGAM375 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM375 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM375 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5211] It is appreciated that VGAM375 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM375 host target genes. The mRNA of each one of this plurality of VGAM375 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM375 RNA, herein designated VGAM RNA, and which when bound by VGAM375 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM375 host target proteins.

[5212] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM375 gene, herein designated VGAM GENE, on one or more VGAM375 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5213] It is yet further appreciated that a function of VGAM375 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM375 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM375 correlate with, and may be deduced from, the identity of the host target genes which VGAM375 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5214] Nucleotide sequences of the VGAM375 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM375 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM375 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM375 are further described hereinbelow with reference to Table 1.

[5215] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM375 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5216] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 376 (VGAM376) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5217] VGAM376 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM376 was detected is described hereinabove with reference to Figs. 2-8.

[5218] VGAM376 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease

virus. VGAM376 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5219] VGAM376 gene, herein designated VGAM GENE, encodes a VGAM376 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM376 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM376 precursor RNA is designated SEQ ID:10011, and is provided hereinbelow with reference to the sequence listing part.

[5220] VGAM376 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5221] An enzyme complex designated DICER COMPLEX, dices

the VGAM376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM376 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM376 RNA is designated SEQ ID:10012, and is provided hereinbelow with reference to the sequence listing part.

[5222] VGAM376 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM376 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM376 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5223] VGAM376 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM376 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM376 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM376 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM376 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5224] The complementary binding of VGAM376 RNA, herein designated VGAM RNA, to host target binding sites on VGAM376 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM376 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM376 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5225] It is appreciated that VGAM376 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM376 host target genes. The mRNA of each one of this plurality of VGAM376 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM376 RNA, herein designated VGAM RNA, and which when bound by VGAM376 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM376 host target proteins.

[5226] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM376 gene, herein designated VGAM GENE, on one or more VGAM376 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5227] It is yet further appreciated that a function of VGAM376 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM376 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM376 correlate with, and may be deduced from, the identity of the host target genes which VGAM376 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5228] Nucleotide sequences of the VGAM376 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM376 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM376 are further described hereinbelow with reference to Table 1.

[5229] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM376 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5230] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 377 (VGAM377) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5231] VGAM377 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM377 was detected is described hereinabove with reference to Figs. 2-8.

[5232] VGAM377 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM377 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[5233] VGAM377 gene, herein designated VGAM GENE, encodes a VGAM377 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM377 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM377 precursor RNA is designated SEQ ID:10016, and is provided hereinbelow with reference to the sequence listing part.

[5234] VGAM377 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM377 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5235] An enzyme complex designated DICER COMPLEX, dices the VGAM377 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM377 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM377 RNA is designated SEQ ID:10017, and is provided hereinbelow with reference to the sequence listing part.

[5236] VGAM377 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM377 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM377 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5237] VGAM377 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM377 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM377 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM377 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM377 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5238] The complementary binding of VGAM377 RNA, herein designated VGAM RNA, to host target binding sites on VGAM377 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM377 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM377 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5239] It is appreciated that VGAM377 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM377 host target genes. The mRNA of each one of this plurality of VGAM377 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM377 RNA, herein designated VGAM RNA, and which when bound by VGAM377 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM377 host target proteins.

[5240] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM377 gene, herein designated VGAM GENE, on one or more VGAM377 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5241] It is yet further appreciated that a function of VGAM377 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM377 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM377 correlate with, and may be deduced from, the identity of the host target genes which VGAM377 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5242] Nucleotide sequences of the VGAM377 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM377 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM377 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM377 are further described hereinbelow with reference to Table 1.

[5243] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM377 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5244] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 378 (VGAM378) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5245] VGAM378 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM378 was detected is described hereinabove with reference to Figs. 2-8.

[5246] VGAM378 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM378 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[5247] VGAM378 gene, herein designated VGAM GENE, encodes a VGAM378 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM378 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM378 precursor RNA is designated SEQ ID:10284, and is provided hereinbelow with reference to the sequence listing part.

[5248] VGAM378 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5249] An enzyme complex designated DICER COMPLEX, dices the VGAM378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM378 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM378 RNA is designated SEQ ID:10285, and is provided hereinbelow with reference to the sequence listing part.

[5250] VGAM378 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM378 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM378 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5251] VGAM378 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM378 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM378 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM378 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM378 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5252] The complementary binding of VGAM378 RNA, herein designated VGAM RNA, to host target binding sites on VGAM378 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM378 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM378 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5253] It is appreciated that VGAM378 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM378 host target genes. The mRNA of each one of this plurality of VGAM378 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM378 RNA, herein designated VGAM RNA, and which when bound by VGAM378 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM378 host target proteins.

[5254] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM378 gene, herein designated VGAM GENE, on one or more VGAM378 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5255] It is yet further appreciated that a function of VGAM378 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM378 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM378 correlate with, and may be deduced from, the identity of the host target genes which VGAM378 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5256] Nucleotide sequences of the VGAM378 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM378 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM378 are further de-

scribed hereinbelow with reference to Table 1.

[5257] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM378 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5258] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 379 (VGAM379) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5259] VGAM379 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM379 was detected is described hereinabove with reference to Figs. 2-8.

[5260] VGAM379 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM379 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5261] VGAM379 gene, herein designated VGAM GENE, encodes a VGAM379 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM379 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM379 precursor RNA is designated SEQ ID:10332, and is provided hereinbelow with reference to the sequence listing part.

[5262] VGAM379 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5263] An enzyme complex designated DICER COMPLEX, dices the VGAM379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM379 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM379 RNA is designated SEQ ID:10333, and is provided hereinbelow with reference to the sequence listing part.

[5264] VGAM379 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM379 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM379 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5265] VGAM379 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM379 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM379 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM379 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM379 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5266] The complementary binding of VGAM379 RNA, herein designated VGAM RNA, to host target binding sites on VGAM379 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM379 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM379 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5267] It is appreciated that VGAM379 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM379 host target genes. The mRNA of each one of this plurality of VGAM379 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM379 RNA, herein designated VGAM RNA, and which when bound by VGAM379 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM379 host target proteins.

[5268] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM379 gene, herein designated VGAM GENE, on one or more VGAM379 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5269] It is yet further appreciated that a function of VGAM379 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM379 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM379 correlate with, and may be deduced from, the identity of the host target genes which VGAM379 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5270] Nucleotide sequences of the VGAM379 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM379 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM379 are further described hereinbelow with reference to Table 1.

[5271] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM379 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5272] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 380 (VGAM380) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5273] VGAM380 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM380 was detected is described hereinabove with reference to Figs. 2-8.

[5274] VGAM380 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM380 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5275] VGAM380 gene, herein designated VGAM GENE, encodes a

VGAM380 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM380 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM380 precursor RNA is designated SEQ ID:10350, and is provided hereinbelow with reference to the sequence listing part.

[5276] VGAM380 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5277] An enzyme complex designated DICER COMPLEX, dices the VGAM380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM380 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM380 RNA is designated SEQ ID:10351, and is provided hereinbelow with reference to the sequence listing part.

[5278] VGAM380 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM380 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM380 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5279] VGAM380 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM380 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM380 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM380 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM380 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5280] The complementary binding of VGAM380 RNA, herein designated VGAM RNA, to host target binding sites on VGAM380 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM380 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM380 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[5281] It is appreciated that VGAM380 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM380 host target genes. The mRNA of each one of this plurality of VGAM380 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM380 RNA, herein designated VGAM RNA, and which when bound by VGAM380 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM380 host target proteins.

[5282] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM380 gene, herein designated VGAM GENE, on one or more VGAM380 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5283] It is yet further appreciated that a function of VGAM380 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM380 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM380 correlate with, and may be deduced from, the identity of the host target genes which VGAM380 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5284] Nucleotide sequences of the VGAM380 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM380 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM380 are further described hereinbelow with reference to Table 1.

[5285] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM380 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5286] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 381 (VGAM381) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5287] VGAM381 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM381 was detected is described hereinabove with reference to Figs. 2-8.

[5288] VGAM381 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM381 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5289] VGAM381 gene, herein designated VGAM GENE, encodes a VGAM381 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM381 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM381 precursor RNA is designated SEQ ID:10385, and is provided hereinbelow with reference to the sequence listing part.

[5290] VGAM381 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5291] An enzyme complex designated DICER COMPLEX, dices the VGAM381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM381 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM381 RNA is designated SEQ ID:10386, and is provided hereinbelow with reference to the sequence listing part.

[5292] VGAM381 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM381 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM381 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5293] VGAM381 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM381 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM381 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM381 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM381 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5294] The complementary binding of VGAM381 RNA, herein designated VGAM RNA, to host target binding sites on VGAM381 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM381 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM381 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5295] It is appreciated that VGAM381 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM381 host target genes. The mRNA of each one of this plurality of VGAM381 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM381 RNA, herein designated VGAM RNA, and which when bound by VGAM381 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM381 host target proteins.

[5296] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM381 gene, herein designated VGAM GENE, on one or more VGAM381 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5297] It is yet further appreciated that a function of VGAM381 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM381 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM381 correlate with, and may be deduced from, the identity of the host target genes which VGAM381 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5298] Nucleotide sequences of the VGAM381 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM381 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM381 are further described hereinbelow with reference to Table 1.

[5299] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM381 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5300] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 382 (VGAM382) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5301] VGAM382 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM382 was detected is described hereinabove with reference to Figs. 2–8.

[5302] VGAM382 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM382 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5303] VGAM382 gene, herein designated VGAM GENE, encodes a VGAM382 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike



most ordinary genes, VGAM382 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM382 precursor RNA is designated SEQ ID:10491, and is provided hereinbelow with reference to the sequence listing part.

[5304] VGAM382 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5305] An enzyme complex designated DICER COMPLEX, dices the VGAM382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM382 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM382 RNA is designated SEQ ID:10492, and is provided hereinbelow with reference to the sequence listing part.

[5306] VGAM382 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM382 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM382 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5307] VGAM382 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM382 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM382 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM382 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM382 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5308] The complementary binding of VGAM382 RNA, herein designated VGAM RNA, to host target binding sites on VGAM382 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM382 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM382 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5309] It is appreciated that VGAM382 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM382 host target genes. The mRNA of each one of this plurality of VGAM382 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM382 RNA, herein designated VGAM RNA, and which when bound by VGAM382 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM382 host target proteins.

[5310] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM382 gene, herein designated VGAM GENE, on one or more VGAM382 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5311] It is yet further appreciated that a function of VGAM382 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM382 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM382 correlate with, and may be deduced from, the identity of the host target genes which VGAM382 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5312] Nucleotide sequences of the VGAM382 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM382 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM382 are further described hereinbelow with reference to Table 1.

[5313] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM382 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5314] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 383 (VGAM383) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5315] VGAM383 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM383 was detected is described hereinabove with reference to Figs. 2–8.

[5316] VGAM383 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM383 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5317] VGAM383 gene, herein designated VGAM GENE, encodes a VGAM383 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM383 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM383 precursor RNA is designated SEQ ID:10522, and is provided hereinbelow with reference to the sequence listing part.

[5318] VGAM383 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5319] An enzyme complex designated DICER COMPLEX, dices the VGAM383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM383 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM383 RNA is designated SEQ ID:10523, and is provided hereinbelow with reference to the sequence listing part.

[5320] VGAM383 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM383 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM383 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5321] VGAM383 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM383 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM383 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM383 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM383 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5322] The complementary binding of VGAM383 RNA, herein designated VGAM RNA, to host target binding sites on VGAM383 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM383 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM383 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5323] It is appreciated that VGAM383 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM383 host target genes. The mRNA of each one of this plurality of VGAM383 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM383 RNA, herein designated VGAM RNA, and which when bound by VGAM383 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM383 host target proteins.

[5324] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM383 gene, herein designated VGAM GENE, on one or more VGAM383 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[5325] It is yet further appreciated that a function of VGAM383 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM383 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM383 correlate with, and may be deduced from, the identity of the host target genes which VGAM383 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5326] Nucleotide sequences of the VGAM383 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM383 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM383 are further described hereinbelow with reference to Table 1.

[5327] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM383 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5328] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 384 (VGAM384) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5329] VGAM384 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM384 was detected is described hereinabove with reference to Figs. 2–8.

[5330] VGAM384 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM384 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5331] VGAM384 gene, herein designated VGAM GENE, encodes a VGAM384 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM384 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM384 precursor RNA is designated SEQ ID:10623, and is provided hereinbelow with reference to the sequence listing part.

[5332] VGAM384 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5333] An enzyme complex designated DICER COMPLEX, dices the VGAM384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM384 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM384 RNA is designated SEQ ID:10624, and is provided hereinbelow with reference to the sequence listing part.

[5334] VGAM384 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM384 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM384 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5335] VGAM384 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM384 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM384 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM384 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM384 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5336] The complementary binding of VGAM384 RNA, herein designated VGAM RNA, to host target binding sites on VGAM384 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM384 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM384 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5337] It is appreciated that VGAM384 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM384 host target genes. The mRNA of

each one of this plurality of VGAM384 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM384 RNA, herein designated VGAM RNA, and which when bound by VGAM384 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM384 host target proteins.

[5338] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM384 gene, herein designated VGAM GENE, on one or more VGAM384 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[5339] It is yet further appreciated that a function of VGAM384 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM384 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM384 correlate with, and may be deduced from, the identity of the host target genes which VGAM384 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5340] Nucleotide sequences of the VGAM384 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM384 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM384 are further described hereinbelow with reference to Table 1.

[5341] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM384 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[5342] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 385 (VGAM385) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5343] VGAM385 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM385 was detected is described hereinabove with reference to Figs. 2–8.

[5344] VGAM385 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM385 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5345] VGAM385 gene, herein designated VGAM GENE, encodes a VGAM385 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM385 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM385 precursor RNA is designated SEQ ID:10685, and is provided hereinbelow with reference to the sequence listing part.

[5346] VGAM385 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM385 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5347] An enzyme complex designated DICER COMPLEX, dices the VGAM385 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM385 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM385 RNA is designated SEQ ID:10686, and

is provided hereinbelow with reference to the sequence listing part.

[5348] VGAM385 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM385 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM385 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5349] VGAM385 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM385 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM385 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM385 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM385 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5350] The complementary binding of VGAM385 RNA, herein designated VGAM RNA, to host target binding sites on VGAM385 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM385 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM385 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5351] It is appreciated that VGAM385 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM385 host target genes. The mRNA of each one of this plurality of VGAM385 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM385 RNA, herein designated VGAM RNA, and which when bound by VGAM385 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM385 host target proteins.

[5352] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM385 gene, herein designated VGAM GENE, on one or more VGAM385 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5353] It is yet further appreciated that a function of VGAM385 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM385 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM385 correlate with, and may be deduced from, the identity of the host target genes which VGAM385 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5354] Nucleotide sequences of the VGAM385 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM385 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM385 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM385 are further described hereinbelow with reference to Table 1.

[5355] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM385 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5356] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 386 (VGAM386) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5357] VGAM386 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM386 was detected is described hereinabove with reference to Figs. 2–8.

[5358] VGAM386 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM386 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5359] VGAM386 gene, herein designated VGAM GENE, encodes a VGAM386 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM386 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM386 precursor RNA is



designated SEQ ID:10691, and is provided hereinbelow with reference to the sequence listing part.

[5360] VGAM386 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM386 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5361] An enzyme complex designated DICER COMPLEX, dices the VGAM386 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM386 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM386 RNA is designated SEQ ID:10692, and is provided hereinbelow with reference to the sequence

listing part.

[5362] VGAM386 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM386 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM386 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5363] VGAM386 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM386 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM386 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM386 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM386 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5364] The complementary binding of VGAM386 RNA, herein designated VGAM RNA, to host target binding sites on VGAM386 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM386 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM386 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5365] It is appreciated that VGAM386 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM386 host target genes. The mRNA of each one of this plurality of VGAM386 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM386 RNA, herein designated VGAM RNA, and which when bound by VGAM386 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM386 host target proteins.

[5366] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM386 gene, herein designated VGAM GENE, on one or more VGAM386 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5367] It is yet further appreciated that a function of VGAM386 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM386 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM386 correlate with, and may be deduced from, the identity of the host target genes which VGAM386 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5368] Nucleotide sequences of the VGAM386 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM386 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM386 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM386 are further described hereinbelow with reference to Table 1.

[5369] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM386 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5370] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 387 (VGAM387) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5371] VGAM387 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM387 was detected is described hereinabove with reference to Figs. 2–8.

[5372] VGAM387 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM387 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5373] VGAM387 gene, herein designated VGAM GENE, encodes a VGAM387 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM387 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM387 precursor RNA is designated SEQ ID:10760, and is provided hereinbelow

with reference to the sequence listing part.

[5374] VGAM387 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5375] An enzyme complex designated DICER COMPLEX, dices the VGAM387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM387 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM387 RNA is designated SEQ ID:10761, and is provided hereinbelow with reference to the sequence listing part.

[5376] VGAM387 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM387 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM387 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5377] VGAM387 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM387 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM387 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM387 RNA, herein designated



VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM387 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5378] The complementary binding of VGAM387 RNA, herein designated VGAM RNA, to host target binding sites on VGAM387 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM387 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM387 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5379] It is appreciated that VGAM387 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM387 host target genes. The mRNA of each one of this plurality of VGAM387 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM387 RNA, herein designated VGAM RNA, and which when bound by VGAM387 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM387 host target proteins.

[5380] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM387 gene, herein designated VGAM GENE, on one or more VGAM387 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5381] It is yet further appreciated that a function of VGAM387 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM387 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM387 correlate with, and may be deduced from, the identity of the host target genes which VGAM387 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5382] Nucleotide sequences of the VGAM387 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM387 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM387 are further described hereinbelow with reference to Table 1.

[5383] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM387 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5384] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 388 (VGAM388) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5385] VGAM388 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM388 was detected is described hereinabove with reference to Figs. 2–8.

[5386] VGAM388 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM388 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5387] VGAM388 gene, herein designated VGAM GENE, encodes a VGAM388 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM388 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM388 precursor RNA is designated SEQ ID:10789, and is provided hereinbelow with reference to the sequence listing part.

[5388] VGAM388 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM388 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5389] An enzyme complex designated DICER COMPLEX, dices the VGAM388 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM388 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM388 RNA is designated SEQ ID:10790, and is provided hereinbelow with reference to the sequence listing part.

[5390] VGAM388 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM388 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM388 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5391] VGAM388 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM388 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM388 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM388 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM388 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5392] The complementary binding of VGAM388 RNA, herein designated VGAM RNA, to host target binding sites on VGAM388 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM388 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM388 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5393] It is appreciated that VGAM388 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM388 host target genes. The mRNA of each one of this plurality of VGAM388 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM388 RNA, herein designated VGAM

RNA, and which when bound by VGAM388 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM388 host target proteins.

[5394] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM388 gene, herein designated VGAM GENE, on one or more VGAM388 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5395] It is yet further appreciated that a function of VGAM388 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM388 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM388 correlate with, and may be deduced from, the identity of the host target genes which VGAM388 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5396] Nucleotide sequences of the VGAM388 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM388 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM388 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM388 are further described hereinbelow with reference to Table 1.

[5397] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM388 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5398] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 389 (VGAM389) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5399] VGAM389 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM389 was detected is described hereinabove with reference to Figs. 2-8.

[5400] VGAM389 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM389 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5401] VGAM389 gene, herein designated VGAM GENE, encodes a VGAM389 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM389 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM389 precursor RNA is designated SEQ ID:10802, and is provided hereinbelow with reference to the sequence listing part.

[5402] VGAM389 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5403] An enzyme complex designated DICER COMPLEX, dices the VGAM389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM389 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM389 RNA is designated SEQ ID:10803, and is provided hereinbelow with reference to the sequence listing part.

[5404] VGAM389 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM389 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM389 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5405] VGAM389 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM389 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM389 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM389 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM389 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5406] The complementary binding of VGAM389 RNA, herein designated VGAM RNA, to host target binding sites on VGAM389 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM389 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM389 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5407] It is appreciated that VGAM389 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM389 host target genes. The mRNA of each one of this plurality of VGAM389 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM389 RNA, herein designated VGAM RNA, and which when bound by VGAM389 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM389 host target proteins.

[5408] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM389 gene, herein designated VGAM GENE, on one or more VGAM389 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5409] It is yet further appreciated that a function of VGAM389 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM389 include diagnosis, prevention and

treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM389 correlate with, and may be deduced from, the identity of the host target genes which VGAM389 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5410] Nucleotide sequences of the VGAM389 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM389 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM389 are further described hereinbelow with reference to Table 1.

[5411] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM389 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5412] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 390 (VGAM390) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5413] VGAM390 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM390 was detected is described hereinabove with reference to Figs. 2–8.

[5414] VGAM390 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM390 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5415] VGAM390 gene, herein designated VGAM GENE, encodes a VGAM390 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM390 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM390 precursor RNA is designated SEQ ID:10847, and is provided hereinbelow with reference to the sequence listing part.

[5416] VGAM390 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM390 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5417] An enzyme complex designated DICER COMPLEX, dices the VGAM390 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM390 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM390 RNA is designated SEQ ID:10848, and is provided hereinbelow with reference to the sequence listing part.

[5418] VGAM390 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM390 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM390 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5419] VGAM390 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM390 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM390 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM390 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM390 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5420] The complementary binding of VGAM390 RNA, herein designated VGAM RNA, to host target binding sites on VGAM390 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM390 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM390 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5421] It is appreciated that VGAM390 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM390 host target genes. The mRNA of each one of this plurality of VGAM390 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM390 RNA, herein designated VGAM RNA, and which when bound by VGAM390 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM390 host target proteins.

[5422] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM390 gene, herein designated VGAM GENE, on one or more VGAM390 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5423] It is yet further appreciated that a function of VGAM390 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM390 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Spe-

cific functions, and accordingly utilities, of VGAM390 correlate with, and may be deduced from, the identity of the host target genes which VGAM390 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5424] Nucleotide sequences of the VGAM390 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM390 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM390 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM390 are further described hereinbelow with reference to Table 1.

[5425] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM390 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5426] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 391 (VGAM391) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[5427] VGAM391 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM391 was detected is described hereinabove with reference to Figs. 2–8.

[5428] VGAM391 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM391 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5429] VGAM391 gene, herein designated VGAM GENE, encodes a VGAM391 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM391 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM391 precursor RNA is designated SEQ ID:10862, and is provided hereinbelow with reference to the sequence listing part.

[5430] VGAM391 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM391 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5431] An enzyme complex designated DICER COMPLEX, dices the VGAM391 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM391 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM391 RNA is designated SEQ ID:10863, and is provided hereinbelow with reference to the sequence listing part.

[5432] VGAM391 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM391 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM391 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5433] VGAM391 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM391 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM391 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM391 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM391 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5434] The complementary binding of VGAM391 RNA, herein designated VGAM RNA, to host target binding sites on VGAM391 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM391 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM391 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5435] It is appreciated that VGAM391 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM391 host target genes. The mRNA of each one of this plurality of VGAM391 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM391 RNA, herein designated VGAM RNA, and which when bound by VGAM391 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM391 host target proteins.

[5436] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM391 gene, herein designated VGAM GENE, on one or more VGAM391 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5437] It is yet further appreciated that a function of VGAM391 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM391 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM391 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM391 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5438] Nucleotide sequences of the VGAM391 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM391 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM391 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM391 are further described hereinbelow with reference to Table 1.

[5439] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM391 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5440] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 392 (VGAM392) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[5441] VGAM392 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM392 was detected is described hereinabove with reference to Figs. 2–8.

[5442] VGAM392 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM392 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5443] VGAM392 gene, herein designated VGAM GENE, encodes a VGAM392 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM392 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM392 precursor RNA is designated SEQ ID:10873, and is provided hereinbelow with reference to the sequence listing part.

[5444] VGAM392 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM392 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5445] An enzyme complex designated DICER COMPLEX, dices the VGAM392 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM392 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM392 RNA is designated SEQ ID:10874, and is provided hereinbelow with reference to the sequence listing part.

[5446] VGAM392 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM392 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM392 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5447] VGAM392 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM392 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM392 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM392 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM392 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5448] The complementary binding of VGAM392 RNA, herein designated VGAM RNA, to host target binding sites on VGAM392 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM392 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM392 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5449] It is appreciated that VGAM392 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM392 host target genes. The mRNA of each one of this plurality of VGAM392 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM392 RNA, herein designated VGAM RNA, and which when bound by VGAM392 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM392 host target proteins.

[5450] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM392 gene, herein designated VGAM GENE, on one or more VGAM392 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5451] It is yet further appreciated that a function of VGAM392 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM392 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM392 correlate with, and may be deduced from, the identity of the



host target genes which VGAM392 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5452] Nucleotide sequences of the VGAM392 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM392 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM392 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM392 are further described hereinbelow with reference to Table 1.

[5453] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM392 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5454] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 393 (VGAM393) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5455] VGAM393 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM393 was detected is described hereinabove with reference to Figs. 2–8.

[5456] VGAM393 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM393 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5457] VGAM393 gene, herein designated VGAM GENE, encodes a VGAM393 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM393 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM393 precursor RNA is designated SEQ ID:10881, and is provided hereinbelow with reference to the sequence listing part.

[5458] VGAM393 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5459] An enzyme complex designated DICER COMPLEX, dices the VGAM393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM393 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM393 RNA is designated SEQ ID:10882, and is provided hereinbelow with reference to the sequence listing part.

[5460] VGAM393 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM393 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM393 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5461] VGAM393 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM393 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM393 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM393 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM393 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5462] The complementary binding of VGAM393 RNA, herein designated VGAM RNA, to host target binding sites on VGAM393 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM393 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM393 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5463] It is appreciated that VGAM393 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM393 host target genes. The mRNA of each one of this plurality of VGAM393 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM393 RNA, herein designated VGAM RNA, and which when bound by VGAM393 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM393 host target proteins.

[5464] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM393 gene, herein designated VGAM GENE, on one or more VGAM393 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5465] It is yet further appreciated that a function of VGAM393 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM393 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM393 correlate with, and may be deduced from, the identity of the host target genes which VGAM393 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[5466] Nucleotide sequences of the VGAM393 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM393 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM393 are further described hereinbelow with reference to Table 1.

[5467] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM393 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5468] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 394 (VGAM394) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5469] VGAM394 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM394 was detected is described hereinabove with reference to Figs. 2–8.

[5470] VGAM394 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM394 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5471] VGAM394 gene, herein designated VGAM GENE, encodes a VGAM394 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM394 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM394 precursor RNA is designated SEQ ID:10898, and is provided hereinbelow with reference to the sequence listing part.

[5472] VGAM394 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the



fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5473] An enzyme complex designated DICER COMPLEX, dices the VGAM394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM394 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM394 RNA is designated SEQ ID:10899, and is provided hereinbelow with reference to the sequence listing part.

[5474] VGAM394 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM394 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM394 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5475] VGAM394 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM394 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM394 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM394 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM394 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[5476] The complementary binding of VGAM394 RNA, herein designated VGAM RNA, to host target binding sites on VGAM394 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM394 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM394 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5477] It is appreciated that VGAM394 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM394 host target genes. The mRNA of each one of this plurality of VGAM394 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM394 RNA, herein designated VGAM RNA, and which when bound by VGAM394 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM394 host target proteins.

[5478] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM394 gene, herein designated VGAM GENE, on one or more VGAM394 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5479] It is yet further appreciated that a function of VGAM394 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM394 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM394 correlate with, and may be deduced from, the identity of the host target genes which VGAM394 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[5480] Nucleotide sequences of the VGAM394 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM394 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM394 are further described hereinbelow with reference to Table 1.

[5481] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM394 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5482] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 395 (VGAM395) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5483] VGAM395 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM395 was detected is described hereinabove with reference to Figs. 2–8.

[5484] VGAM395 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM395 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5485] VGAM395 gene, herein designated VGAM GENE, encodes a VGAM395 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM395 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM395 precursor RNA is designated SEQ ID:11117, and is provided hereinbelow with reference to the sequence listing part.

[5486] VGAM395 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5487] An enzyme complex designated DICER COMPLEX, dices the VGAM395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM395 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM395 RNA is designated SEQ ID:11118, and is provided hereinbelow with reference to the sequence listing part.

[5488] VGAM395 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM395 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM395 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[5489] VGAM395 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM395 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM395 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM395 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM395 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[5490] The complementary binding of VGAM395 RNA, herein designated VGAM RNA, to host target binding sites on VGAM395 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM395 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM395 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5491] It is appreciated that VGAM395 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM395 host target genes. The mRNA of each one of this plurality of VGAM395 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM395 RNA, herein designated VGAM RNA, and which when bound by VGAM395 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM395 host target proteins.

[5492] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM395 gene, herein designated VGAM GENE, on one or

more VGAM395 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5493] It is yet further appreciated that a function of VGAM395 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM395 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM395 correlate with, and may be deduced from, the identity of the host target genes which VGAM395 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5494] Nucleotide sequences of the VGAM395 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM395 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM395 are further described hereinbelow with reference to Table 1.

[5495] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM395 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5496] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 396 (VGAM396) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5497] VGAM396 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM396 was detected is described

hereinabove with reference to Figs. 2–8.

[5498] VGAM396 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM396 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5499] VGAM396 gene, herein designated VGAM GENE, encodes a VGAM396 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM396 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM396 precursor RNA is designated SEQ ID:11122, and is provided hereinbelow with reference to the sequence listing part.

[5500] VGAM396 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5501] An enzyme complex designated DICER COMPLEX, dices the VGAM396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM396 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM396 RNA is designated SEQ ID:11123, and is provided hereinbelow with reference to the sequence listing part.

[5502] VGAM396 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM396 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM396 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5503] VGAM396 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM396 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM396 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM396 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM396 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5504] The complementary binding of VGAM396 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM396 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM396 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM396 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5505] It is appreciated that VGAM396 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM396 host target genes. The mRNA of each one of this plurality of VGAM396 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM396 RNA, herein designated VGAM RNA, and which when bound by VGAM396 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM396 host target proteins.

[5506] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM396 gene, herein designated VGAM GENE, on one or more VGAM396 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5507] It is yet further appreciated that a function of VGAM396 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM396 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM396 correlate with, and may be deduced from, the identity of the host target genes which VGAM396 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5508] Nucleotide sequences of the VGAM396 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM396 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM396 are further described hereinbelow with reference to Table 1.

[5509] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM396 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5510] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 397 (VGAM397) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5511] VGAM397 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM397 was detected is described hereinabove with reference to Figs. 2-8.

[5512] VGAM397 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM397 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5513] VGAM397 gene, herein designated VGAM GENE, encodes a VGAM397 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM397 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM397 precursor RNA is designated SEQ ID:11270, and is provided hereinbelow with reference to the sequence listing part.

[5514] VGAM397 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM397 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[5515] An enzyme complex designated DICER COMPLEX, dices the VGAM397 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM397 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM397 RNA is designated SEQ ID:11271, and is provided hereinbelow with reference to the sequence listing part.

[5516] VGAM397 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM397 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM397 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5517] VGAM397 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM397 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM397 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM397 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM397 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5518] The complementary binding of VGAM397 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM397 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM397 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM397 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5519] It is appreciated that VGAM397 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM397 host target genes. The mRNA of each one of this plurality of VGAM397 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM397 RNA, herein designated VGAM RNA, and which when bound by VGAM397 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM397 host target proteins.

[5520] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM397 gene, herein designated VGAM GENE, on one or more VGAM397 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5521] It is yet further appreciated that a function of VGAM397 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM397 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM397 correlate with, and may be deduced from, the identity of the host target genes which VGAM397 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5522] Nucleotide sequences of the VGAM397 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM397 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM397 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM397 are further described hereinbelow with reference to Table 1.

[5523] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM397 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5524] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 398 (VGAM398) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5525] VGAM398 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM398 was detected is described hereinabove with reference to Figs. 2-8.

[5526] VGAM398 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 2. VGAM398 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5527] VGAM398 gene, herein designated VGAM GENE, encodes a VGAM398 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM398 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM398 precursor RNA is designated SEQ ID:11413, and is provided hereinbelow with reference to the sequence listing part.

[5528] VGAM398 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[5529] An enzyme complex designated DICER COMPLEX, dices the VGAM398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM398 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM398 RNA is designated SEQ ID:11414, and is provided hereinbelow with reference to the sequence listing part.

[5530] VGAM398 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM398 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM398 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5531] VGAM398 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM398 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM398 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM398 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM398 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5532] The complementary binding of VGAM398 RNA, herein designated VGAM RNA, to host target binding sites on VGAM398 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM398 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM398 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5533] It is appreciated that VGAM398 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM398 host target genes. The mRNA of each one of this plurality of VGAM398 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM398 RNA, herein designated VGAM RNA, and which when bound by VGAM398 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM398 host target proteins.

[5534] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM398 gene, herein designated VGAM GENE, on one or more VGAM398 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5535] It is yet further appreciated that a function of VGAM398 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM398 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM398 correlate with, and may be deduced from, the identity of the host target genes which VGAM398 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5536] Nucleotide sequences of the VGAM398 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM398 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM398 are further described hereinbelow with reference to Table 1.

[5537] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM398 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5538] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 399 (VGAM399) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5539] VGAM399 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM399 was detected is described hereinabove with reference to Figs. 2-8.

[5540] VGAM399 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2.

VGAM399 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5541] VGAM399 gene, herein designated VGAM GENE, encodes a VGAM399 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM399 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM399 precursor RNA is designated SEQ ID:11428, and is provided hereinbelow with reference to the sequence listing part.

[5542] VGAM399 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5543] An enzyme complex designated DICER COMPLEX, dices

the VGAM399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM399 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM399 RNA is designated SEQ ID:11429, and is provided hereinbelow with reference to the sequence listing part.

[5544] VGAM399 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM399 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM399 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5545] VGAM399 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM399 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM399 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM399 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM399 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5546] The complementary binding of VGAM399 RNA, herein designated VGAM RNA, to host target binding sites on VGAM399 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and



BINDING SITE III, inhibits translation of VGAM399 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM399 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5547] It is appreciated that VGAM399 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM399 host target genes. The mRNA of each one of this plurality of VGAM399 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM399 RNA, herein designated VGAM RNA, and which when bound by VGAM399 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM399 host target proteins.

[5548] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM399 gene, herein designated VGAM GENE, on one or more VGAM399 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5549] It is yet further appreciated that a function of VGAM399 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM399 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM399 correlate with, and may be deduced from, the identity of the host target genes which VGAM399 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5550] Nucleotide sequences of the VGAM399 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM399 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM399 are further described hereinbelow with reference to Table 1.

[5551] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM399 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5552] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 400 (VGAM400) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5553] VGAM400 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM400 was detected is described hereinabove with reference to Figs. 2-8.

[5554] VGAM400 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM400 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[5555] VGAM400 gene, herein designated VGAM GENE, encodes a VGAM400 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM400 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM400 precursor RNA is designated SEQ ID:11547, and is provided hereinbelow with reference to the sequence listing part.

[5556] VGAM400 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM400 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5557] An enzyme complex designated DICER COMPLEX, dices the VGAM400 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM400 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM400 RNA is designated SEQ ID:11548, and is provided hereinbelow with reference to the sequence listing part.

[5558] VGAM400 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM400 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM400 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5559] VGAM400 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM400 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM400 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM400 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM400 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5560] The complementary binding of VGAM400 RNA, herein designated VGAM RNA, to host target binding sites on VGAM400 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM400 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM400 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5561] It is appreciated that VGAM400 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM400 host target genes. The mRNA of each one of this plurality of VGAM400 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM400 RNA, herein designated VGAM RNA, and which when bound by VGAM400 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM400 host target proteins.

[5562] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM400 gene, herein designated VGAM GENE, on one or more VGAM400 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5563] It is yet further appreciated that a function of VGAM400 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM400 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM400 correlate with, and may be deduced from, the identity of the host target genes which VGAM400 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5564] Nucleotide sequences of the VGAM400 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM400 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM400 folded precursor RNA, herein designated VGAM



FOLDED PRECURSOR RNA, of VGAM400 are further described hereinbelow with reference to Table 1.

[5565] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM400 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5566] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 401 (VGAM401) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5567] VGAM401 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM401 was detected is described hereinabove with reference to Figs. 2-8.

[5568] VGAM401 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM401 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[5569] VGAM401 gene, herein designated VGAM GENE, encodes a VGAM401 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM401 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM401 precursor RNA is designated SEQ ID:11613, and is provided hereinbelow with reference to the sequence listing part.

[5570] VGAM401 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5571] An enzyme complex designated DICER COMPLEX, dices the VGAM401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM401 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM401 RNA is designated SEQ ID:11614, and is provided hereinbelow with reference to the sequence listing part.

[5572] VGAM401 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM401 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM401 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5573] VGAM401 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM401 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM401 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM401 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM401 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5574] The complementary binding of VGAM401 RNA, herein designated VGAM RNA, to host target binding sites on VGAM401 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM401 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM401 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5575] It is appreciated that VGAM401 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM401 host target genes. The mRNA of each one of this plurality of VGAM401 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM401 RNA, herein designated VGAM RNA, and which when bound by VGAM401 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM401 host target proteins.

[5576] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM401 gene, herein designated VGAM GENE, on one or more VGAM401 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5577] It is yet further appreciated that a function of VGAM401 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM401 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM401 correlate with, and may be deduced from, the identity of the host target genes which VGAM401 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5578] Nucleotide sequences of the VGAM401 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM401 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM401 are further de-

scribed hereinbelow with reference to Table 1.

[5579] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM401 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5580] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 402 (VGAM402) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5581] VGAM402 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM402 was detected is described hereinabove with reference to Figs. 2-8.

[5582] VGAM402 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM402 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5583] VGAM402 gene, herein designated VGAM GENE, encodes a VGAM402 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM402 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM402 precursor RNA is designated SEQ ID:11620, and is provided hereinbelow with reference to the sequence listing part.

[5584] VGAM402 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM402 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5585] An enzyme complex designated DICER COMPLEX, dices the VGAM402 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM402 RNA, herein designated VGAM RNA, a single stranded ~22 nt



long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM402 RNA is designated SEQ ID:8404, and is provided hereinbelow with reference to the sequence listing part.

[5586] VGAM402 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM402 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM402 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5587] VGAM402 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM402 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM402 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM402 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM402 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5588] The complementary binding of VGAM402 RNA, herein designated VGAM RNA, to host target binding sites on VGAM402 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM402 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM402 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5589] It is appreciated that VGAM402 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM402 host target genes. The mRNA of each one of this plurality of VGAM402 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM402 RNA, herein designated VGAM RNA, and which when bound by VGAM402 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM402 host target proteins.

[5590] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM402 gene, herein designated VGAM GENE, on one or more VGAM402 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5591] It is yet further appreciated that a function of VGAM402 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM402 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM402 correlate with, and may be deduced from, the identity of the host target genes which VGAM402 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5592] Nucleotide sequences of the VGAM402 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM402 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM402 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM402 are further described hereinbelow with reference to Table 1.

[5593] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM402 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5594] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 403 (VGAM403) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5595] VGAM403 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM403 was detected is described hereinabove with reference to Figs. 2-8.

[5596] VGAM403 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM403 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5597] VGAM403 gene, herein designated VGAM GENE, encodes a

VGAM403 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM403 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM403 precursor RNA is designated SEQ ID:11621, and is provided hereinbelow with reference to the sequence listing part.

[5598] VGAM403 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5599] An enzyme complex designated DICER COMPLEX, dices the VGAM403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM403 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM403 RNA is designated SEQ ID:11622, and is provided hereinbelow with reference to the sequence listing part.

[5600] VGAM403 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM403 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM403 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5601] VGAM403 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM403 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM403 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM403 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM403 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5602] The complementary binding of VGAM403 RNA, herein designated VGAM RNA, to host target binding sites on VGAM403 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM403 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM403 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein



is therefore outlined by a broken line.

[5603] It is appreciated that VGAM403 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM403 host target genes. The mRNA of each one of this plurality of VGAM403 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM403 RNA, herein designated VGAM RNA, and which when bound by VGAM403 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM403 host target proteins.

[5604] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM403 gene, herein designated VGAM GENE, on one or more VGAM403 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5605] It is yet further appreciated that a function of VGAM403 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM403 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM403 correlate with, and may be deduced from, the identity of the host target genes which VGAM403 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5606] Nucleotide sequences of the VGAM403 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM403 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM403 are further described hereinbelow with reference to Table 1.

[5607] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM403 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5608] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 404 (VGAM404) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5609] VGAM404 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM404 was detected is described hereinabove with reference to Figs. 2-8.

[5610] VGAM404 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Southern bean mosaic virus. VGAM404 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5611] VGAM404 gene, herein designated VGAM GENE, encodes a VGAM404 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM404 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM404 precursor RNA is designated SEQ ID:11641, and is provided hereinbelow with reference to the sequence listing part.

[5612] VGAM404 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5613] An enzyme complex designated DICER COMPLEX, dices the VGAM404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM404 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM404 RNA is designated SEQ ID:11642, and is provided hereinbelow with reference to the sequence listing part.

[5614] VGAM404 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM404 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM404 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5615] VGAM404 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM404 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM404 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM404 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM404 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5616] The complementary binding of VGAM404 RNA, herein designated VGAM RNA, to host target binding sites on VGAM404 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM404 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM404 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5617] It is appreciated that VGAM404 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM404 host target genes. The mRNA of each one of this plurality of VGAM404 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM404 RNA, herein designated VGAM RNA, and which when bound by VGAM404 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM404 host target proteins.

[5618] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM404 gene, herein designated VGAM GENE, on one or more VGAM404 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5619] It is yet further appreciated that a function of VGAM404 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM404 include diagnosis, prevention and treatment of viral infection by Southern bean mosaic virus. Specific functions, and accordingly utilities, of VGAM404 correlate with, and may be deduced from, the identity of the host target genes which VGAM404 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5620] Nucleotide sequences of the VGAM404 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM404 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM404 are further described hereinbelow with reference to Table 1.

[5621] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of



Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM404 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5622] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 405 (VGAM405) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5623] VGAM405 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM405 was detected is described hereinabove with reference to Figs. 2–8.

[5624] VGAM405 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Southern bean mosaic virus. VGAM405 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5625] VGAM405 gene, herein designated VGAM GENE, encodes a VGAM405 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM405 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM405 precursor RNA is designated SEQ ID:11655, and is provided hereinbelow with reference to the sequence listing part.

[5626] VGAM405 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM405 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5627] An enzyme complex designated DICER COMPLEX, dices the VGAM405 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM405 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM405 RNA is designated SEQ ID:11656, and is provided hereinbelow with reference to the sequence listing part.

[5628] VGAM405 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM405 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM405 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5629] VGAM405 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM405 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM405 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM405 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM405 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5630] The complementary binding of VGAM405 RNA, herein designated VGAM RNA, to host target binding sites on VGAM405 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM405 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM405 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5631] It is appreciated that VGAM405 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM405 host target genes. The mRNA of each one of this plurality of VGAM405 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM405 RNA, herein designated VGAM RNA, and which when bound by VGAM405 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM405 host target proteins.

[5632] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM405 gene, herein designated VGAM GENE, on one or more VGAM405 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5633] It is yet further appreciated that a function of VGAM405 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM405 include diagnosis, prevention and treatment of viral infection by Southern bean mosaic virus. Specific functions, and accordingly utilities, of VGAM405 correlate with, and may be deduced from, the identity of the host target genes which VGAM405 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5634] Nucleotide sequences of the VGAM405 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM405 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM405 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM405 are further described hereinbelow with reference to Table 1.

[5635] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM405 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5636] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 406 (VGAM406) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5637] VGAM406 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM406 was detected is described hereinabove with reference to Figs. 2–8.

[5638] VGAM406 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM406 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5639] VGAM406 gene, herein designated VGAM GENE, encodes a VGAM406 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM406 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM406 precursor RNA is designated SEQ ID:11670, and is provided hereinbelow with reference to the sequence listing part.

[5640] VGAM406 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM406 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5641] An enzyme complex designated DICER COMPLEX, dices the VGAM406 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM406 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other



necessary proteins. A probable (over 28%) nucleotide sequence of VGAM406 RNA is designated SEQ ID:11671, and is provided hereinbelow with reference to the sequence listing part.

[5642] VGAM406 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM406 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM406 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5643] VGAM406 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM406 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM406 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM406 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM406 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5644] The complementary binding of VGAM406 RNA, herein designated VGAM RNA, to host target binding sites on VGAM406 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM406 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM406 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5645] It is appreciated that VGAM406 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM406 host target genes. The mRNA of each one of this plurality of VGAM406 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM406 RNA, herein designated VGAM RNA, and which when bound by VGAM406 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM406 host target proteins.

[5646] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM406 gene, herein designated VGAM GENE, on one or more VGAM406 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[5647] It is yet further appreciated that a function of VGAM406 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM406 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM406 correlate with, and may be deduced from, the identity of the host target genes which VGAM406 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5648] Nucleotide sequences of the VGAM406 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM406 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM406 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM406 are further described hereinbelow with reference to Table 1.

[5649] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM406 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5650] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 407 (VGAM407) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5651] VGAM407 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM407 was detected is described hereinabove with reference to Figs. 2–8.

[5652] VGAM407 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM407 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5653] VGAM407 gene, herein designated VGAM GENE, encodes a VGAM407 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM407 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM407 precursor RNA is designated SEQ ID:11760, and is provided hereinbelow with reference to the sequence listing part.

[5654] VGAM407 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5655] An enzyme complex designated DICER COMPLEX, dices the VGAM407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM407 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM407 RNA is designated SEQ ID:11761, and is provided hereinbelow with reference to the sequence listing part.

[5656] VGAM407 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM407 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM407 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5657] VGAM407 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM407 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM407 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM407 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM407 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5658] The complementary binding of VGAM407 RNA, herein designated VGAM RNA, to host target binding sites on VGAM407 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM407 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM407 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5659] It is appreciated that VGAM407 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM407 host target genes. The mRNA of



each one of this plurality of VGAM407 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM407 RNA, herein designated VGAM RNA, and which when bound by VGAM407 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM407 host target proteins.

[5660] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM407 gene, herein designated VGAM GENE, on one or more VGAM407 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[5661] It is yet further appreciated that a function of VGAM407 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM407 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM407 correlate with, and may be deduced from, the identity of the host target genes which VGAM407 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5662] Nucleotide sequences of the VGAM407 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM407 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM407 are further described hereinbelow with reference to Table 1.

[5663] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM407 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[5664] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 408 (VGAM408) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5665] VGAM408 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM408 was detected is described hereinabove with reference to Figs. 2–8.

[5666] VGAM408 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Southern bean mosaic virus. VGAM408 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5667] VGAM408 gene, herein designated VGAM GENE, encodes a VGAM408 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM408 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM408 precursor RNA is designated SEQ ID:11765, and is provided hereinbelow with reference to the sequence listing part.

[5668] VGAM408 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5669] An enzyme complex designated DICER COMPLEX, dices the VGAM408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM408 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM408 RNA is designated SEQ ID:11766, and

is provided hereinbelow with reference to the sequence listing part.

[5670] VGAM408 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM408 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM408 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5671] VGAM408 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM408 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM408 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM408 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM408 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5672] The complementary binding of VGAM408 RNA, herein designated VGAM RNA, to host target binding sites on VGAM408 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM408 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM408 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5673] It is appreciated that VGAM408 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM408 host target genes. The mRNA of each one of this plurality of VGAM408 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM408 RNA, herein designated VGAM RNA, and which when bound by VGAM408 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM408 host target proteins.

[5674] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM408 gene, herein designated VGAM GENE, on one or more VGAM408 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5675] It is yet further appreciated that a function of VGAM408 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM408 include diagnosis, prevention and treatment of viral infection by Southern bean mosaic virus. Specific functions, and accordingly utilities, of VGAM408 correlate with, and may be deduced from, the identity of the host target genes which VGAM408 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5676] Nucleotide sequences of the VGAM408 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM408 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM408 are further described hereinbelow with reference to Table 1.

[5677] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM408 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.



[5678] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 409 (VGAM409) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5679] VGAM409 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM409 was detected is described hereinabove with reference to Figs. 2–8.

[5680] VGAM409 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Southern bean mosaic virus. VGAM409 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5681] VGAM409 gene, herein designated VGAM GENE, encodes a VGAM409 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM409 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM409 precursor RNA is

designated SEQ ID:11850, and is provided hereinbelow with reference to the sequence listing part.

[5682] VGAM409 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM409 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5683] An enzyme complex designated DICER COMPLEX, dices the VGAM409 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM409 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM409 RNA is designated SEQ ID:11851, and is provided hereinbelow with reference to the sequence

listing part.

[5684] VGAM409 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM409 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM409 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5685] VGAM409 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM409 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM409 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM409 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM409 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5686] The complementary binding of VGAM409 RNA, herein designated VGAM RNA, to host target binding sites on VGAM409 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM409 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM409 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5687] It is appreciated that VGAM409 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM409 host target genes. The mRNA of each one of this plurality of VGAM409 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM409 RNA, herein designated VGAM RNA, and which when bound by VGAM409 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM409 host target proteins.

[5688] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM409 gene, herein designated VGAM GENE, on one or more VGAM409 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5689] It is yet further appreciated that a function of VGAM409 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM409 include diagnosis, prevention and treatment of viral infection by Southern bean mosaic virus. Specific functions, and accordingly utilities, of VGAM409 correlate with, and may be deduced from, the identity of the host target genes which VGAM409 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5690] Nucleotide sequences of the VGAM409 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM409 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM409 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM409 are further described hereinbelow with reference to Table 1.

[5691] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM409 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5692] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 410 (VGAM410) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5693] VGAM410 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM410 was detected is described hereinabove with reference to Figs. 2–8.

[5694] VGAM410 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM410 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5695] VGAM410 gene, herein designated VGAM GENE, encodes a VGAM410 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM410 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM410 precursor RNA is designated SEQ ID:11861, and is provided hereinbelow

with reference to the sequence listing part.

[5696] VGAM410 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5697] An enzyme complex designated DICER COMPLEX, dices the VGAM410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM410 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM410 RNA is designated SEQ ID:11862, and is provided hereinbelow with reference to the sequence listing part.



[5698] VGAM410 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM410 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM410 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5699] VGAM410 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM410 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM410 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM410 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM410 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5700] The complementary binding of VGAM410 RNA, herein designated VGAM RNA, to host target binding sites on VGAM410 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM410 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM410 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5701] It is appreciated that VGAM410 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM410 host target genes. The mRNA of each one of this plurality of VGAM410 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM410 RNA, herein designated VGAM RNA, and which when bound by VGAM410 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM410 host target proteins.

[5702] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM410 gene, herein designated VGAM GENE, on one or more VGAM410 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5703] It is yet further appreciated that a function of VGAM410 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM410 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM410 correlate with, and may be deduced from, the identity of the host target genes which VGAM410 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5704] Nucleotide sequences of the VGAM410 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM410 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM410 are further described hereinbelow with reference to Table 1.

[5705] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM410 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5706] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 411 (VGAM411) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5707] VGAM411 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM411 was detected is described hereinabove with reference to Figs. 2–8.

[5708] VGAM411 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM411 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5709] VGAM411 gene, herein designated VGAM GENE, encodes a VGAM411 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM411 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM411 precursor RNA is designated SEQ ID:11874, and is provided hereinbelow with reference to the sequence listing part.

[5710] VGAM411 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5711] An enzyme complex designated DICER COMPLEX, dices the VGAM411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM411 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM411 RNA is designated SEQ ID:11875, and is provided hereinbelow with reference to the sequence listing part.

[5712] VGAM411 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM411 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM411 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5713] VGAM411 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM411 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM411 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM411 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM411 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5714] The complementary binding of VGAM411 RNA, herein designated VGAM RNA, to host target binding sites on VGAM411 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM411 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM411 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5715] It is appreciated that VGAM411 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM411 host target genes. The mRNA of each one of this plurality of VGAM411 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM411 RNA, herein designated VGAM



RNA, and which when bound by VGAM411 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM411 host target proteins.

[5716] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM411 gene, herein designated VGAM GENE, on one or more VGAM411 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5717] It is yet further appreciated that a function of VGAM411 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM411 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM411 correlate with, and may be deduced from, the identity of the host target genes which VGAM411 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5718] Nucleotide sequences of the VGAM411 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM411 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM411 are further described hereinbelow with reference to Table 1.

[5719] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM411 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5720] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 412 (VGAM412) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5721] VGAM412 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM412 was detected is described hereinabove with reference to Figs. 2-8.

[5722] VGAM412 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM412 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5723] VGAM412 gene, herein designated VGAM GENE, encodes a VGAM412 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM412 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM412 precursor RNA is designated SEQ ID:11877, and is provided hereinbelow with reference to the sequence listing part.

[5724] VGAM412 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5725] An enzyme complex designated DICER COMPLEX, dices the VGAM412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM412 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM412 RNA is designated SEQ ID:11878, and is provided hereinbelow with reference to the sequence listing part.

[5726] VGAM412 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM412 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM412 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5727] VGAM412 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM412 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM412 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM412 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM412 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5728] The complementary binding of VGAM412 RNA, herein designated VGAM RNA, to host target binding sites on VGAM412 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM412 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM412 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5729] It is appreciated that VGAM412 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM412 host target genes. The mRNA of each one of this plurality of VGAM412 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM412 RNA, herein designated VGAM RNA, and which when bound by VGAM412 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM412 host target proteins.

[5730] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM412 gene, herein designated VGAM GENE, on one or more VGAM412 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5731] It is yet further appreciated that a function of VGAM412 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM412 include diagnosis, prevention and

treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM412 correlate with, and may be deduced from, the identity of the host target genes which VGAM412 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5732] Nucleotide sequences of the VGAM412 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM412 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM412 are further described hereinbelow with reference to Table 1.

[5733] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM412 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5734] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 413 (VGAM413) viral gene, which modulates ex-



pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5735] VGAM413 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM413 was detected is described hereinabove with reference to Figs. 2–8.

[5736] VGAM413 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM413 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5737] VGAM413 gene, herein designated VGAM GENE, encodes a VGAM413 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM413 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM413 precursor RNA is designated SEQ ID:11891, and is provided hereinbelow with reference to the sequence listing part.

[5738] VGAM413 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM413 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5739] An enzyme complex designated DICER COMPLEX, dices the VGAM413 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM413 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM413 RNA is designated SEQ ID:11892, and is provided hereinbelow with reference to the sequence listing part.

[5740] VGAM413 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM413 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM413 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5741] VGAM413 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM413 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM413 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM413 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM413 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5742] The complementary binding of VGAM413 RNA, herein designated VGAM RNA, to host target binding sites on VGAM413 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM413 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM413 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5743] It is appreciated that VGAM413 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM413 host target genes. The mRNA of each one of this plurality of VGAM413 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM413 RNA, herein designated VGAM RNA, and which when bound by VGAM413 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM413 host target proteins.

[5744] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM413 gene, herein designated VGAM GENE, on one or more VGAM413 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5745] It is yet further appreciated that a function of VGAM413 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM413 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria

Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM413 correlate with, and may be deduced from, the identity of the host target genes which VGAM413 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5746] Nucleotide sequences of the VGAM413 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM413 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM413 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM413 are further described hereinbelow with reference to Table 1.

[5747] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM413 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5748] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 414 (VGAM414) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[5749] VGAM414 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM414 was detected is described hereinabove with reference to Figs. 2–8.

[5750] VGAM414 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM414 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5751] VGAM414 gene, herein designated VGAM GENE, encodes a VGAM414 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM414 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM414 precursor RNA is designated SEQ ID:11904, and is provided hereinbelow with reference to the sequence listing part.

[5752] VGAM414 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM414 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5753] An enzyme complex designated DICER COMPLEX, dices the VGAM414 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM414 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM414 RNA is designated SEQ ID:11905, and is provided hereinbelow with reference to the sequence listing part.

[5754] VGAM414 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM414 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM414 host target RNA, herein



designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5755] VGAM414 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM414 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM414 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM414 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM414 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5756] The complementary binding of VGAM414 RNA, herein designated VGAM RNA, to host target binding sites on VGAM414 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM414 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM414 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5757] It is appreciated that VGAM414 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM414 host target genes. The mRNA of each one of this plurality of VGAM414 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM414 RNA, herein designated VGAM RNA, and which when bound by VGAM414 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM414 host target proteins.

[5758] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM414 gene, herein designated VGAM GENE, on one or more VGAM414 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5759] It is yet further appreciated that a function of VGAM414 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM414 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM414 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM414 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5760] Nucleotide sequences of the VGAM414 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM414 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM414 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM414 are further described hereinbelow with reference to Table 1.

[5761] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM414 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5762] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 415 (VGAM415) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[5763] VGAM415 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM415 was detected is described hereinabove with reference to Figs. 2–8.

[5764] VGAM415 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM415 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5765] VGAM415 gene, herein designated VGAM GENE, encodes a VGAM415 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM415 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM415 precursor RNA is designated SEQ ID:11927, and is provided hereinbelow with reference to the sequence listing part.

[5766] VGAM415 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM415 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5767] An enzyme complex designated DICER COMPLEX, dices the VGAM415 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM415 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM415 RNA is designated SEQ ID:11928, and is provided hereinbelow with reference to the sequence listing part.

[5768] VGAM415 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM415 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM415 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5769] VGAM415 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM415 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM415 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM415 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM415 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5770] The complementary binding of VGAM415 RNA, herein designated VGAM RNA, to host target binding sites on VGAM415 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM415 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM415 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5771] It is appreciated that VGAM415 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM415 host target genes. The mRNA of each one of this plurality of VGAM415 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM415 RNA, herein designated VGAM RNA, and which when bound by VGAM415 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM415 host target proteins.

[5772] It is further appreciated by one skilled in the art that the



mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM415 gene, herein designated VGAM GENE, on one or more VGAM415 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5773] It is yet further appreciated that a function of VGAM415 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM415 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM415 correlate with, and may be deduced from, the identity of the

host target genes which VGAM415 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5774] Nucleotide sequences of the VGAM415 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM415 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM415 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM415 are further described hereinbelow with reference to Table 1.

[5775] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM415 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5776] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 416 (VGAM416) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5777] VGAM416 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM416 was detected is described hereinabove with reference to Figs. 2–8.

[5778] VGAM416 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM416 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5779] VGAM416 gene, herein designated VGAM GENE, encodes a VGAM416 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM416 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM416 precursor RNA is designated SEQ ID:11950, and is provided hereinbelow with reference to the sequence listing part.

[5780] VGAM416 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5781] An enzyme complex designated DICER COMPLEX, dices the VGAM416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM416 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM416 RNA is designated SEQ ID:11951, and is provided hereinbelow with reference to the sequence listing part.

[5782] VGAM416 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM416 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM416 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5783] VGAM416 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM416 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM416 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM416 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM416 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5784] The complementary binding of VGAM416 RNA, herein designated VGAM RNA, to host target binding sites on VGAM416 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM416 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM416 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5785] It is appreciated that VGAM416 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM416 host target genes. The mRNA of each one of this plurality of VGAM416 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM416 RNA, herein designated VGAM RNA, and which when bound by VGAM416 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM416 host target proteins.

[5786] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM416 gene, herein designated VGAM GENE, on one or more VGAM416 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5787] It is yet further appreciated that a function of VGAM416 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM416 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM416 correlate with, and may be deduced from, the identity of the host target genes which VGAM416 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[5788] Nucleotide sequences of the VGAM416 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM416 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM416 are further described hereinbelow with reference to Table 1.

[5789] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM416 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5790] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 417 (VGAM417) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5791] VGAM417 is a novel bioinformatically detected regulatory,



non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM417 was detected is described hereinabove with reference to Figs. 2–8.

[5792] VGAM417 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM417 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5793] VGAM417 gene, herein designated VGAM GENE, encodes a VGAM417 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM417 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM417 precursor RNA is designated SEQ ID:11989, and is provided hereinbelow with reference to the sequence listing part.

[5794] VGAM417 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM417 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5795] An enzyme complex designated DICER COMPLEX, dices the VGAM417 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM417 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM417 RNA is designated SEQ ID:11990, and is provided hereinbelow with reference to the sequence listing part.

[5796] VGAM417 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM417 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM417 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5797] VGAM417 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM417 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM417 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM417 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM417 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[5798] The complementary binding of VGAM417 RNA, herein designated VGAM RNA, to host target binding sites on VGAM417 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM417 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM417 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5799] It is appreciated that VGAM417 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM417 host target genes. The mRNA of each one of this plurality of VGAM417 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM417 RNA, herein designated VGAM RNA, and which when bound by VGAM417 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM417 host target proteins.

[5800] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM417 gene, herein designated VGAM GENE, on one or more VGAM417 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5801] It is yet further appreciated that a function of VGAM417 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM417 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM417 correlate with, and may be deduced from, the identity of the host target genes which VGAM417 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[5802] Nucleotide sequences of the VGAM417 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM417 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM417 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM417 are further described hereinbelow with reference to Table 1.

[5803] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM417 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5804] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 418 (VGAM418) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5805] VGAM418 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM418 was detected is described hereinabove with reference to Figs. 2–8.

[5806] VGAM418 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM418 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5807] VGAM418 gene, herein designated VGAM GENE, encodes a VGAM418 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM418 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM418 precursor RNA is designated SEQ ID:11996, and is provided hereinbelow with reference to the sequence listing part.

[5808] VGAM418 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5809] An enzyme complex designated DICER COMPLEX, dices the VGAM418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM418 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM418 RNA is designated SEQ ID:11997, and is provided hereinbelow with reference to the sequence listing part.

[5810] VGAM418 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM418 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM418 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and



3UTR respectively.

[5811] VGAM418 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM418 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM418 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM418 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM418 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5812] The complementary binding of VGAM418 RNA, herein designated VGAM RNA, to host target binding sites on VGAM418 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM418 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM418 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5813] It is appreciated that VGAM418 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM418 host target genes. The mRNA of each one of this plurality of VGAM418 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM418 RNA, herein designated VGAM RNA, and which when bound by VGAM418 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM418 host target proteins.

[5814] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM418 gene, herein designated VGAM GENE, on one or

more VGAM418 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5815] It is yet further appreciated that a function of VGAM418 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM418 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM418 correlate with, and may be deduced from, the identity of the host target genes which VGAM418 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5816] Nucleotide sequences of the VGAM418 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM418 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM418 are further described hereinbelow with reference to Table 1.

[5817] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM418 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5818] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 419 (VGAM419) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5819] VGAM419 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM419 was detected is described

hereinabove with reference to Figs. 2–8.

[5820] VGAM419 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM419 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5821] VGAM419 gene, herein designated VGAM GENE, encodes a VGAM419 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM419 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM419 precursor RNA is designated SEQ ID:12039, and is provided hereinbelow with reference to the sequence listing part.

[5822] VGAM419 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM419 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5823] An enzyme complex designated DICER COMPLEX, dices the VGAM419 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM419 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM419 RNA is designated SEQ ID:12040, and is provided hereinbelow with reference to the sequence listing part.

[5824] VGAM419 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM419 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM419 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5825] VGAM419 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM419 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM419 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM419 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM419 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5826] The complementary binding of VGAM419 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM419 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM419 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM419 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5827] It is appreciated that VGAM419 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM419 host target genes. The mRNA of each one of this plurality of VGAM419 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM419 RNA, herein designated VGAM RNA, and which when bound by VGAM419 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM419 host target proteins.

[5828] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM419 gene, herein designated VGAM GENE, on one or more VGAM419 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5829] It is yet further appreciated that a function of VGAM419 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM419 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM419 correlate with, and may be deduced from, the identity of the host target genes which VGAM419 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5830] Nucleotide sequences of the VGAM419 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM419 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM419 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM419 are further described hereinbelow with reference to Table 1.

[5831] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM419 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5832] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 420 (VGAM420) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5833] VGAM420 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM420 was detected is described hereinabove with reference to Figs. 2-8.

[5834] VGAM420 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM420 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5835] VGAM420 gene, herein designated VGAM GENE, encodes a VGAM420 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM420 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM420 precursor RNA is designated SEQ ID:12120, and is provided hereinbelow with reference to the sequence listing part.

[5836] VGAM420 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[5837] An enzyme complex designated DICER COMPLEX, dices the VGAM420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM420 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM420 RNA is designated SEQ ID:12121, and is provided hereinbelow with reference to the sequence listing part.

[5838] VGAM420 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM420 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM420 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5839] VGAM420 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM420 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM420 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM420 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM420 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5840] The complementary binding of VGAM420 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM420 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM420 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM420 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5841] It is appreciated that VGAM420 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM420 host target genes. The mRNA of each one of this plurality of VGAM420 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM420 RNA, herein designated VGAM RNA, and which when bound by VGAM420 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM420 host target proteins.

[5842] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM420 gene, herein designated VGAM GENE, on one or more VGAM420 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5843] It is yet further appreciated that a function of VGAM420 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM420 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM420 correlate with, and may be deduced from, the identity of the host target genes which VGAM420 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5844] Nucleotide sequences of the VGAM420 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM420 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM420 are further described hereinbelow with reference to Table 1.

[5845] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM420 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5846] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 421 (VGAM421) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5847] VGAM421 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM421 was detected is described hereinabove with reference to Figs. 2-8.

[5848] VGAM421 gene, herein designated VGAM GENE, is a viral



gene contained in the genome of Human herpesvirus 8. VGAM421 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5849] VGAM421 gene, herein designated VGAM GENE, encodes a VGAM421 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM421 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM421 precursor RNA is designated SEQ ID:12135, and is provided hereinbelow with reference to the sequence listing part.

[5850] VGAM421 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5851] An enzyme complex designated DICER COMPLEX, dices the VGAM421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM421 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM421 RNA is designated SEQ ID:12136, and is provided hereinbelow with reference to the sequence listing part.

[5852] VGAM421 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM421 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM421 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5853] VGAM421 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM421 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM421 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM421 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM421 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5854] The complementary binding of VGAM421 RNA, herein designated VGAM RNA, to host target binding sites on VGAM421 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM421 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM421 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5855] It is appreciated that VGAM421 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM421 host target genes. The mRNA of each one of this plurality of VGAM421 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM421 RNA, herein designated VGAM RNA, and which when bound by VGAM421 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM421 host target proteins.

[5856] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM421 gene, herein designated VGAM GENE, on one or more VGAM421 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5857] It is yet further appreciated that a function of VGAM421 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM421 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM421 correlate with, and may be deduced from, the identity of the host target genes which VGAM421 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5858] Nucleotide sequences of the VGAM421 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM421 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM421 are further described hereinbelow with reference to Table 1.

[5859] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM421 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5860] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 422 (VGAM422) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5861] VGAM422 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM422 was detected is described hereinabove with reference to Figs. 2-8.

[5862] VGAM422 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8.

VGAM422 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5863] VGAM422 gene, herein designated VGAM GENE, encodes a VGAM422 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM422 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM422 precursor RNA is designated SEQ ID:12183, and is provided hereinbelow with reference to the sequence listing part.

[5864] VGAM422 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5865] An enzyme complex designated DICER COMPLEX, dices

the VGAM422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM422 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM422 RNA is designated SEQ ID:12184, and is provided hereinbelow with reference to the sequence listing part.

[5866] VGAM422 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM422 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM422 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5867] VGAM422 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM422 host target



RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM422 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM422 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM422 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5868] The complementary binding of VGAM422 RNA, herein designated VGAM RNA, to host target binding sites on VGAM422 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM422 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM422 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5869] It is appreciated that VGAM422 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM422 host target genes. The mRNA of each one of this plurality of VGAM422 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM422 RNA, herein designated VGAM RNA, and which when bound by VGAM422 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM422 host target proteins.

[5870] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM422 gene, herein designated VGAM GENE, on one or more VGAM422 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5871] It is yet further appreciated that a function of VGAM422 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM422 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM422 correlate with, and may be deduced from, the identity of the host target genes which VGAM422 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5872] Nucleotide sequences of the VGAM422 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM422 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM422 are further described hereinbelow with reference to Table 1.

[5873] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM422 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5874] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 423 (VGAM423) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5875] VGAM423 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM423 was detected is described hereinabove with reference to Figs. 2-8.

[5876] VGAM423 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM423 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[5877] VGAM423 gene, herein designated VGAM GENE, encodes a VGAM423 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM423 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM423 precursor RNA is designated SEQ ID:12187, and is provided hereinbelow with reference to the sequence listing part.

[5878] VGAM423 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM423 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5879] An enzyme complex designated DICER COMPLEX, dices the VGAM423 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM423 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM423 RNA is designated SEQ ID:12188, and is provided hereinbelow with reference to the sequence listing part.

[5880] VGAM423 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM423 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM423 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5881] VGAM423 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM423 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM423 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM423 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM423 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5882] The complementary binding of VGAM423 RNA, herein designated VGAM RNA, to host target binding sites on VGAM423 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM423 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM423 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5883] It is appreciated that VGAM423 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM423 host target genes. The mRNA of each one of this plurality of VGAM423 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM423 RNA, herein designated VGAM RNA, and which when bound by VGAM423 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM423 host target proteins.

[5884] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM423 gene, herein designated VGAM GENE, on one or more VGAM423 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated



only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5885] It is yet further appreciated that a function of VGAM423 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM423 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM423 correlate with, and may be deduced from, the identity of the host target genes which VGAM423 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5886] Nucleotide sequences of the VGAM423 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM423 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM423 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM423 are further described hereinbelow with reference to Table 1.

[5887] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM423 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5888] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 424 (VGAM424) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5889] VGAM424 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM424 was detected is described hereinabove with reference to Figs. 2-8.

[5890] VGAM424 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM424 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[5891] VGAM424 gene, herein designated VGAM GENE, encodes a VGAM424 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM424 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM424 precursor RNA is designated SEQ ID:12203, and is provided hereinbelow with reference to the sequence listing part.

[5892] VGAM424 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5893] An enzyme complex designated DICER COMPLEX, dices the VGAM424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM424 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM424 RNA is designated SEQ ID:12204, and is provided hereinbelow with reference to the sequence listing part.

[5894] VGAM424 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM424 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM424 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5895] VGAM424 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM424 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM424 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM424 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM424 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5896] The complementary binding of VGAM424 RNA, herein designated VGAM RNA, to host target binding sites on VGAM424 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM424 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM424 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5897] It is appreciated that VGAM424 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM424 host target genes. The mRNA of each one of this plurality of VGAM424 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM424 RNA, herein designated VGAM RNA, and which when bound by VGAM424 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM424 host target proteins.

[5898] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM424 gene, herein designated VGAM GENE, on one or more VGAM424 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5899] It is yet further appreciated that a function of VGAM424 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM424 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM424 correlate with, and may be deduced from, the identity of the host target genes which VGAM424 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5900] Nucleotide sequences of the VGAM424 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM424 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM424 are further de-

scribed hereinbelow with reference to Table 1.

[5901] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM424 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5902] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 425 (VGAM425) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5903] VGAM425 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM425 was detected is described hereinabove with reference to Figs. 2-8.

[5904] VGAM425 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM425 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.



[5905] VGAM425 gene, herein designated VGAM GENE, encodes a VGAM425 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM425 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM425 precursor RNA is designated SEQ ID:12221, and is provided hereinbelow with reference to the sequence listing part.

[5906] VGAM425 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5907] An enzyme complex designated DICER COMPLEX, dices the VGAM425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM425 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM425 RNA is designated SEQ ID:12222, and is provided hereinbelow with reference to the sequence listing part.

[5908] VGAM425 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM425 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM425 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5909] VGAM425 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM425 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM425 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM425 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM425 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5910] The complementary binding of VGAM425 RNA, herein designated VGAM RNA, to host target binding sites on VGAM425 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM425 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM425 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5911] It is appreciated that VGAM425 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM425 host target genes. The mRNA of each one of this plurality of VGAM425 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM425 RNA, herein designated VGAM RNA, and which when bound by VGAM425 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM425 host target proteins.

[5912] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM425 gene, herein designated VGAM GENE, on one or more VGAM425 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5913] It is yet further appreciated that a function of VGAM425 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM425 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM425 correlate with, and may be deduced from, the identity of the host target genes which VGAM425 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5914] Nucleotide sequences of the VGAM425 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM425 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM425 are further described hereinbelow with reference to Table 1.

[5915] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM425 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5916] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 426 (VGAM426) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5917] VGAM426 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM426 was detected is described hereinabove with reference to Figs. 2-8.

[5918] VGAM426 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM426 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5919] VGAM426 gene, herein designated VGAM GENE, encodes a

VGAM426 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM426 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM426 precursor RNA is designated SEQ ID:12236, and is provided hereinbelow with reference to the sequence listing part.

[5920] VGAM426 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5921] An enzyme complex designated DICER COMPLEX, dices the VGAM426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM426 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM426 RNA is designated SEQ ID:12237, and is provided hereinbelow with reference to the sequence listing part.

[5922] VGAM426 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM426 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM426 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5923] VGAM426 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM426 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM426 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed



sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM426 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM426 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5924] The complementary binding of VGAM426 RNA, herein designated VGAM RNA, to host target binding sites on VGAM426 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM426 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM426 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[5925] It is appreciated that VGAM426 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM426 host target genes. The mRNA of each one of this plurality of VGAM426 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM426 RNA, herein designated VGAM RNA, and which when bound by VGAM426 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM426 host target proteins.

[5926] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM426 gene, herein designated VGAM GENE, on one or more VGAM426 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5927] It is yet further appreciated that a function of VGAM426 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM426 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM426 correlate with, and may be deduced from, the identity of the host target genes which VGAM426 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5928] Nucleotide sequences of the VGAM426 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM426 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM426 are further described hereinbelow with reference to Table 1.

[5929] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM426 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5930] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 427 (VGAM427) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5931] VGAM427 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM427 was detected is described hereinabove with reference to Figs. 2-8.

[5932] VGAM427 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM427 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5933] VGAM427 gene, herein designated VGAM GENE, encodes a VGAM427 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM427 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM427 precursor RNA is designated SEQ ID:12263, and is provided hereinbelow with reference to the sequence listing part.

[5934] VGAM427 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5935] An enzyme complex designated DICER COMPLEX, dices the VGAM427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM427 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM427 RNA is designated SEQ ID:12264, and is provided hereinbelow with reference to the sequence listing part.

[5936] VGAM427 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM427 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM427 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5937] VGAM427 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM427 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM427 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM427 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM427 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5938] The complementary binding of VGAM427 RNA, herein designated VGAM RNA, to host target binding sites on VGAM427 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM427 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM427 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5939] It is appreciated that VGAM427 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM427 host target genes. The mRNA of each one of this plurality of VGAM427 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM427 RNA, herein designated VGAM RNA, and which when bound by VGAM427 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM427 host target proteins.

[5940] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM427 gene, herein designated VGAM GENE, on one or more VGAM427 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-



though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5941] It is yet further appreciated that a function of VGAM427 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM427 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM427 correlate with, and may be deduced from, the identity of the host target genes which VGAM427 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5942] Nucleotide sequences of the VGAM427 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM427 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM427 are further described hereinbelow with reference to Table 1.

[5943] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM427 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5944] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 428 (VGAM428) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5945] VGAM428 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM428 was detected is described hereinabove with reference to Figs. 2–8.

[5946] VGAM428 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM428 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5947] VGAM428 gene, herein designated VGAM GENE, encodes a VGAM428 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM428 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM428 precursor RNA is designated SEQ ID:12275, and is provided hereinbelow with reference to the sequence listing part.

[5948] VGAM428 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM428 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5949] An enzyme complex designated DICER COMPLEX, dices the VGAM428 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM428 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM428 RNA is designated SEQ ID:12276, and is provided hereinbelow with reference to the sequence listing part.

[5950] VGAM428 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM428 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM428 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5951] VGAM428 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM428 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM428 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM428 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM428 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5952] The complementary binding of VGAM428 RNA, herein designated VGAM RNA, to host target binding sites on VGAM428 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM428 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM428 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5953] It is appreciated that VGAM428 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM428 host target genes. The mRNA of each one of this plurality of VGAM428 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM428 RNA, herein designated VGAM RNA, and which when bound by VGAM428 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM428 host target proteins.

[5954] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM428 gene, herein designated VGAM GENE, on one or more VGAM428 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[5955] It is yet further appreciated that a function of VGAM428 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM428 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM428 correlate with, and may be deduced from, the identity of the host target genes which VGAM428 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5956] Nucleotide sequences of the VGAM428 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM428 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM428 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM428 are further described hereinbelow with reference to Table 1.

[5957] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM428 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5958] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 429 (VGAM429) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5959] VGAM429 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM429 was detected is described hereinabove with reference to Figs. 2–8.

[5960] VGAM429 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM429 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5961] VGAM429 gene, herein designated VGAM GENE, encodes a VGAM429 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM429 precursor RNA, herein



designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM429 precursor RNA is designated SEQ ID:12278, and is provided hereinbelow with reference to the sequence listing part.

[5962] VGAM429 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM429 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5963] An enzyme complex designated DICER COMPLEX, dices the VGAM429 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM429 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM429 RNA is designated SEQ ID:12279, and is provided hereinbelow with reference to the sequence listing part.

[5964] VGAM429 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM429 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM429 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5965] VGAM429 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM429 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM429 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM429 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM429 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5966] The complementary binding of VGAM429 RNA, herein designated VGAM RNA, to host target binding sites on VGAM429 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM429 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM429 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5967] It is appreciated that VGAM429 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM429 host target genes. The mRNA of each one of this plurality of VGAM429 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM429 RNA, herein designated VGAM RNA, and which when bound by VGAM429 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM429 host target proteins.

[5968] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM429 gene, herein designated VGAM GENE, on one or more VGAM429 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[5969] It is yet further appreciated that a function of VGAM429 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM429 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM429 correlate with, and may be deduced from, the identity of the host target genes which VGAM429 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5970] Nucleotide sequences of the VGAM429 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM429 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM429 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM429 are further described hereinbelow with reference to Table 1.

[5971] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM429 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[5972] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 430 (VGAM430) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5973] VGAM430 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM430 was detected is described hereinabove with reference to Figs. 2–8.

[5974] VGAM430 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM430 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5975] VGAM430 gene, herein designated VGAM GENE, encodes a VGAM430 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM430 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM430 precursor RNA is designated SEQ ID:12291, and is provided hereinbelow with reference to the sequence listing part.

[5976] VGAM430 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5977] An enzyme complex designated DICER COMPLEX, dices the VGAM430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM430 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM430 RNA is designated SEQ ID:12292, and is provided hereinbelow with reference to the sequence listing part.

[5978] VGAM430 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM430 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM430 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5979] VGAM430 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM430 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM430 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-



preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM430 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM430 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5980] The complementary binding of VGAM430 RNA, herein designated VGAM RNA, to host target binding sites on VGAM430 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM430 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM430 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5981] It is appreciated that VGAM430 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM430 host target genes. The mRNA of

each one of this plurality of VGAM430 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM430 RNA, herein designated VGAM RNA, and which when bound by VGAM430 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM430 host target proteins.

[5982] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM430 gene, herein designated VGAM GENE, on one or more VGAM430 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[5983] It is yet further appreciated that a function of VGAM430 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM430 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM430 correlate with, and may be deduced from, the identity of the host target genes which VGAM430 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5984] Nucleotide sequences of the VGAM430 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM430 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM430 are further described hereinbelow with reference to Table 1.

[5985] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM430 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[5986] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 431 (VGAM431) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[5987] VGAM431 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM431 was detected is described hereinabove with reference to Figs. 2–8.

[5988] VGAM431 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM431 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[5989] VGAM431 gene, herein designated VGAM GENE, encodes a VGAM431 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM431 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM431 precursor RNA is designated SEQ ID:12314, and is provided hereinbelow with reference to the sequence listing part.

[5990] VGAM431 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[5991] An enzyme complex designated DICER COMPLEX, dices the VGAM431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM431 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM431 RNA is designated SEQ ID:12315, and

is provided hereinbelow with reference to the sequence listing part.

[5992] VGAM431 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM431 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM431 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[5993] VGAM431 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM431 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM431 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM431 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM431 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[5994] The complementary binding of VGAM431 RNA, herein designated VGAM RNA, to host target binding sites on VGAM431 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM431 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM431 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[5995] It is appreciated that VGAM431 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM431 host target genes. The mRNA of each one of this plurality of VGAM431 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM431 RNA, herein designated VGAM RNA, and which when bound by VGAM431 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM431 host target proteins.

[5996] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM431 gene, herein designated VGAM GENE, on one or more VGAM431 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).



[5997] It is yet further appreciated that a function of VGAM431 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM431 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM431 correlate with, and may be deduced from, the identity of the host target genes which VGAM431 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[5998] Nucleotide sequences of the VGAM431 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM431 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM431 are further described hereinbelow with reference to Table 1.

[5999] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM431 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6000] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 432 (VGAM432) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6001] VGAM432 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM432 was detected is described hereinabove with reference to Figs. 2–8.

[6002] VGAM432 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM432 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6003] VGAM432 gene, herein designated VGAM GENE, encodes a VGAM432 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM432 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM432 precursor RNA is

designated SEQ ID:12342, and is provided hereinbelow with reference to the sequence listing part.

[6004] VGAM432 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6005] An enzyme complex designated DICER COMPLEX, dices the VGAM432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM432 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM432 RNA is designated SEQ ID:12343, and is provided hereinbelow with reference to the sequence

listing part.

[6006] VGAM432 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM432 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM432 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6007] VGAM432 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM432 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM432 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM432 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM432 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6008] The complementary binding of VGAM432 RNA, herein designated VGAM RNA, to host target binding sites on VGAM432 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM432 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM432 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6009] It is appreciated that VGAM432 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM432 host target genes. The mRNA of each one of this plurality of VGAM432 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM432 RNA, herein designated VGAM RNA, and which when bound by VGAM432 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM432 host target proteins.

[6010] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM432 gene, herein designated VGAM GENE, on one or more VGAM432 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6011] It is yet further appreciated that a function of VGAM432 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM432 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM432 correlate with, and may be deduced from, the identity of the host target genes which VGAM432 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6012] Nucleotide sequences of the VGAM432 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM432 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM432 are further described hereinbelow with reference to Table 1.

[6013] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM432 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6014] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 433 (VGAM433) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6015] VGAM433 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM433 was detected is described hereinabove with reference to Figs. 2–8.

[6016] VGAM433 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM433 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6017] VGAM433 gene, herein designated VGAM GENE, encodes a VGAM433 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM433 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM433 precursor RNA is designated SEQ ID:12417, and is provided hereinbelow



with reference to the sequence listing part.

[6018] VGAM433 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6019] An enzyme complex designated DICER COMPLEX, dices the VGAM433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM433 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM433 RNA is designated SEQ ID:12418, and is provided hereinbelow with reference to the sequence listing part.

[6020] VGAM433 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM433 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM433 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6021] VGAM433 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM433 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM433 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM433 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM433 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6022] The complementary binding of VGAM433 RNA, herein designated VGAM RNA, to host target binding sites on VGAM433 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM433 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM433 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6023] It is appreciated that VGAM433 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM433 host target genes. The mRNA of each one of this plurality of VGAM433 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM433 RNA, herein designated VGAM RNA, and which when bound by VGAM433 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM433 host target proteins.

[6024] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM433 gene, herein designated VGAM GENE, on one or more VGAM433 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6025] It is yet further appreciated that a function of VGAM433 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM433 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM433 correlate with, and may be deduced from, the identity of the host target genes which VGAM433 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6026] Nucleotide sequences of the VGAM433 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM433 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM433 are further described hereinbelow with reference to Table 1.

[6027] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM433 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6028] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 434 (VGAM434) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6029] VGAM434 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM434 was detected is described hereinabove with reference to Figs. 2–8.

[6030] VGAM434 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM434 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6031] VGAM434 gene, herein designated VGAM GENE, encodes a VGAM434 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM434 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM434 precursor RNA is designated SEQ ID:12421, and is provided hereinbelow with reference to the sequence listing part.

[6032] VGAM434 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6033] An enzyme complex designated DICER COMPLEX, dices the VGAM434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM434 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM434 RNA is designated SEQ ID:12422, and is provided hereinbelow with reference to the sequence listing part.

[6034] VGAM434 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM434 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM434 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6035] VGAM434 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM434 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM434 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM434 RNA, herein designated VGAM RNA, may have a different number of host target



binding sites in untranslated regions of a VGAM434 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6036] The complementary binding of VGAM434 RNA, herein designated VGAM RNA, to host target binding sites on VGAM434 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM434 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM434 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6037] It is appreciated that VGAM434 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM434 host target genes. The mRNA of each one of this plurality of VGAM434 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM434 RNA, herein designated VGAM

RNA, and which when bound by VGAM434 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM434 host target proteins.

[6038] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM434 gene, herein designated VGAM GENE, on one or more VGAM434 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6039] It is yet further appreciated that a function of VGAM434 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM434 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM434 correlate with, and may be deduced from, the identity of the host target genes which VGAM434 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6040] Nucleotide sequences of the VGAM434 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM434 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM434 are further described hereinbelow with reference to Table 1.

[6041] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM434 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6042] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 435 (VGAM435) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6043] VGAM435 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM435 was detected is described hereinabove with reference to Figs. 2–8.

[6044] VGAM435 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM435 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6045] VGAM435 gene, herein designated VGAM GENE, encodes a VGAM435 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM435 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM435 precursor RNA is designated SEQ ID:12434, and is provided hereinbelow with reference to the sequence listing part.

[6046] VGAM435 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6047] An enzyme complex designated DICER COMPLEX, dices the VGAM435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM435 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM435 RNA is designated SEQ ID:12435, and is provided hereinbelow with reference to the sequence listing part.

[6048] VGAM435 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM435 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM435 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6049] VGAM435 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM435 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM435 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM435 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM435 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6050] The complementary binding of VGAM435 RNA, herein designated VGAM RNA, to host target binding sites on VGAM435 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM435 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM435 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6051] It is appreciated that VGAM435 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM435 host target genes. The mRNA of each one of this plurality of VGAM435 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM435 RNA, herein designated VGAM RNA, and which when bound by VGAM435 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM435 host target proteins.

[6052] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM435 gene, herein designated VGAM GENE, on one or more VGAM435 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6053] It is yet further appreciated that a function of VGAM435 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM435 include diagnosis, prevention and



treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM435 correlate with, and may be deduced from, the identity of the host target genes which VGAM435 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6054] Nucleotide sequences of the VGAM435 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM435 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM435 are further described hereinbelow with reference to Table 1.

[6055] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM435 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6056] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 436 (VGAM436) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6057] VGAM436 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM436 was detected is described hereinabove with reference to Figs. 2–8.

[6058] VGAM436 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM436 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6059] VGAM436 gene, herein designated VGAM GENE, encodes a VGAM436 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM436 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM436 precursor RNA is designated SEQ ID:12453, and is provided hereinbelow with reference to the sequence listing part.

[6060] VGAM436 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM436 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6061] An enzyme complex designated DICER COMPLEX, dices the VGAM436 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM436 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM436 RNA is designated SEQ ID:12454, and is provided hereinbelow with reference to the sequence listing part.

[6062] VGAM436 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM436 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM436 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6063] VGAM436 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM436 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM436 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM436 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM436 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6064] The complementary binding of VGAM436 RNA, herein designated VGAM RNA, to host target binding sites on VGAM436 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM436 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM436 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6065] It is appreciated that VGAM436 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM436 host target genes. The mRNA of each one of this plurality of VGAM436 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM436 RNA, herein designated VGAM RNA, and which when bound by VGAM436 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM436 host target proteins.

[6066] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM436 gene, herein designated VGAM GENE, on one or more VGAM436 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6067] It is yet further appreciated that a function of VGAM436 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM436 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Spe-

cific functions, and accordingly utilities, of VGAM436 correlate with, and may be deduced from, the identity of the host target genes which VGAM436 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6068] Nucleotide sequences of the VGAM436 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM436 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM436 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM436 are further described hereinbelow with reference to Table 1.

[6069] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM436 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6070] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 437 (VGAM437) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[6071] VGAM437 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM437 was detected is described hereinabove with reference to Figs. 2–8.

[6072] VGAM437 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM437 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6073] VGAM437 gene, herein designated VGAM GENE, encodes a VGAM437 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM437 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM437 precursor RNA is designated SEQ ID:12461, and is provided hereinbelow with reference to the sequence listing part.

[6074] VGAM437 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM437 folded precursor RNA, herein designated VGAM FOLDED PRECUR-



SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6075] An enzyme complex designated DICER COMPLEX, dices the VGAM437 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM437 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM437 RNA is designated SEQ ID:12462, and is provided hereinbelow with reference to the sequence listing part.

[6076] VGAM437 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM437 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM437 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6077] VGAM437 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM437 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM437 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM437 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM437 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6078] The complementary binding of VGAM437 RNA, herein designated VGAM RNA, to host target binding sites on VGAM437 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM437 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM437 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6079] It is appreciated that VGAM437 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM437 host target genes. The mRNA of each one of this plurality of VGAM437 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM437 RNA, herein designated VGAM RNA, and which when bound by VGAM437 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM437 host target proteins.

[6080] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM437 gene, herein designated VGAM GENE, on one or more VGAM437 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6081] It is yet further appreciated that a function of VGAM437 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM437 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM437 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM437 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6082] Nucleotide sequences of the VGAM437 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM437 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM437 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM437 are further described hereinbelow with reference to Table 1.

[6083] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM437 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6084] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 438 (VGAM438) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[6085] VGAM438 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM438 was detected is described hereinabove with reference to Figs. 2–8.

[6086] VGAM438 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM438 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6087] VGAM438 gene, herein designated VGAM GENE, encodes a VGAM438 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM438 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM438 precursor RNA is designated SEQ ID:12469, and is provided hereinbelow with reference to the sequence listing part.

[6088] VGAM438 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM438 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6089] An enzyme complex designated DICER COMPLEX, dices the VGAM438 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM438 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM438 RNA is designated SEQ ID:12470, and is provided hereinbelow with reference to the sequence listing part.

[6090] VGAM438 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM438 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM438 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6091] VGAM438 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM438 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM438 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM438 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM438 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an



example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6092] The complementary binding of VGAM438 RNA, herein designated VGAM RNA, to host target binding sites on VGAM438 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM438 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM438 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6093] It is appreciated that VGAM438 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM438 host target genes. The mRNA of each one of this plurality of VGAM438 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM438 RNA, herein designated VGAM RNA, and which when bound by VGAM438 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM438 host target proteins.

[6094] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM438 gene, herein designated VGAM GENE, on one or more VGAM438 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6095] It is yet further appreciated that a function of VGAM438 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM438 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM438 correlate with, and may be deduced from, the identity of the

host target genes which VGAM438 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6096] Nucleotide sequences of the VGAM438 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM438 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM438 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM438 are further described hereinbelow with reference to Table 1.

[6097] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM438 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6098] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 439 (VGAM439) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6099] VGAM439 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM439 was detected is described hereinabove with reference to Figs. 2–8.

[6100] VGAM439 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM439 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6101] VGAM439 gene, herein designated VGAM GENE, encodes a VGAM439 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM439 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM439 precursor RNA is designated SEQ ID:12493, and is provided hereinbelow with reference to the sequence listing part.

[6102] VGAM439 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6103] An enzyme complex designated DICER COMPLEX, dices the VGAM439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM439 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM439 RNA is designated SEQ ID:12494, and is provided hereinbelow with reference to the sequence listing part.

[6104] VGAM439 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM439 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM439 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6105] VGAM439 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM439 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM439 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM439 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM439 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6106] The complementary binding of VGAM439 RNA, herein designated VGAM RNA, to host target binding sites on VGAM439 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM439 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM439 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6107] It is appreciated that VGAM439 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM439 host target genes. The mRNA of each one of this plurality of VGAM439 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM439 RNA, herein designated VGAM RNA, and which when bound by VGAM439 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM439 host target proteins.

[6108] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM439 gene, herein designated VGAM GENE, on one or more VGAM439 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6109] It is yet further appreciated that a function of VGAM439 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM439 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM439 correlate with, and may be deduced from, the identity of the host target genes which VGAM439 binds and inhibits, and



the function of these host target genes, as elaborated hereinbelow.

[6110] Nucleotide sequences of the VGAM439 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM439 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM439 are further described hereinbelow with reference to Table 1.

[6111] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM439 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6112] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 440 (VGAM440) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6113] VGAM440 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM440 was detected is described hereinabove with reference to Figs. 2–8.

[6114] VGAM440 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM440 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6115] VGAM440 gene, herein designated VGAM GENE, encodes a VGAM440 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM440 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM440 precursor RNA is designated SEQ ID:12513, and is provided hereinbelow with reference to the sequence listing part.

[6116] VGAM440 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6117] An enzyme complex designated DICER COMPLEX, dices the VGAM440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM440 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM440 RNA is designated SEQ ID:12514, and is provided hereinbelow with reference to the sequence listing part.

[6118] VGAM440 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM440 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM440 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6119] VGAM440 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM440 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM440 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM440 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM440 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[6120] The complementary binding of VGAM440 RNA, herein designated VGAM RNA, to host target binding sites on VGAM440 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM440 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM440 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6121] It is appreciated that VGAM440 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM440 host target genes. The mRNA of each one of this plurality of VGAM440 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM440 RNA, herein designated VGAM RNA, and which when bound by VGAM440 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM440 host target proteins.

[6122] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM440 gene, herein designated VGAM GENE, on one or more VGAM440 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6123] It is yet further appreciated that a function of VGAM440 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM440 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM440 correlate with, and may be deduced from, the identity of the host target genes which VGAM440 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[6124] Nucleotide sequences of the VGAM440 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM440 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM440 are further described hereinbelow with reference to Table 1.

[6125] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM440 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6126] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 441 (VGAM441) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6127] VGAM441 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM441 was detected is described hereinabove with reference to Figs. 2–8.

[6128] VGAM441 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM441 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6129] VGAM441 gene, herein designated VGAM GENE, encodes a VGAM441 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM441 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM441 precursor RNA is designated SEQ ID:12520, and is provided hereinbelow with reference to the sequence listing part.

[6130] VGAM441 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the



RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6131] An enzyme complex designated DICER COMPLEX, dices the VGAM441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM441 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM441 RNA is designated SEQ ID:12521, and is provided hereinbelow with reference to the sequence listing part.

[6132] VGAM441 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM441 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM441 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3'UTR respectively.

[6133] VGAM441 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM441 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM441 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM441 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM441 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6134] The complementary binding of VGAM441 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM441 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM441 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM441 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6135] It is appreciated that VGAM441 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM441 host target genes. The mRNA of each one of this plurality of VGAM441 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM441 RNA, herein designated VGAM RNA, and which when bound by VGAM441 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM441 host target proteins.

[6136] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM441 gene, herein designated VGAM GENE, on one or more VGAM441 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6137] It is yet further appreciated that a function of VGAM441 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM441 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM441 correlate with, and may be deduced from, the identity of the host target genes which VGAM441 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6138] Nucleotide sequences of the VGAM441 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM441 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM441 are further described hereinbelow with reference to Table 1.

[6139] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM441 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6140] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 442 (VGAM442) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6141] VGAM442 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM442 was detected is described hereinabove with reference to Figs. 2-8.

[6142] VGAM442 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM442 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6143] VGAM442 gene, herein designated VGAM GENE, encodes a VGAM442 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM442 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM442 precursor RNA is designated SEQ ID:12524, and is provided hereinbelow with reference to the sequence listing part.

[6144] VGAM442 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[6145] An enzyme complex designated DICER COMPLEX, dices the VGAM442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM442 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM442 RNA is designated SEQ ID:12525, and is provided hereinbelow with reference to the sequence listing part.

[6146] VGAM442 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM442 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM442 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6147] VGAM442 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM442 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM442 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM442 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM442 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6148] The complementary binding of VGAM442 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM442 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM442 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM442 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6149] It is appreciated that VGAM442 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM442 host target genes. The mRNA of each one of this plurality of VGAM442 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM442 RNA, herein designated VGAM RNA, and which when bound by VGAM442 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM442 host target proteins.

[6150] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM442 gene, herein designated VGAM GENE, on one or more VGAM442 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6151] It is yet further appreciated that a function of VGAM442 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM442 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM442 correlate with, and may be deduced from, the identity of the host target genes which VGAM442 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6152] Nucleotide sequences of the VGAM442 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM442 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM442 are further described hereinbelow with reference to Table 1.

[6153] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM442 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6154] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 443 (VGAM443) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6155] VGAM443 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM443 was detected is described hereinabove with reference to Figs. 2-8.

[6156] VGAM443 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 6. VGAM443 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6157] VGAM443 gene, herein designated VGAM GENE, encodes a VGAM443 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM443 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM443 precursor RNA is designated SEQ ID:12542, and is provided hereinbelow with reference to the sequence listing part.

[6158] VGAM443 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6159] An enzyme complex designated DICER COMPLEX, dices the VGAM443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM443 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM443 RNA is designated SEQ ID:12543, and is provided hereinbelow with reference to the sequence listing part.

[6160] VGAM443 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM443 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM443 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6161] VGAM443 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM443 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM443 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM443 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM443 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6162] The complementary binding of VGAM443 RNA, herein designated VGAM RNA, to host target binding sites on VGAM443 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM443 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM443 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6163] It is appreciated that VGAM443 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM443 host target genes. The mRNA of each one of this plurality of VGAM443 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM443 RNA, herein designated VGAM RNA, and which when bound by VGAM443 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM443 host target proteins.

[6164] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM443 gene, herein designated VGAM GENE, on one or more VGAM443 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6165] It is yet further appreciated that a function of VGAM443 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM443 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM443 correlate with, and may be deduced from, the identity of the host target genes which VGAM443 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6166] Nucleotide sequences of the VGAM443 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM443 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM443 are further described hereinbelow with reference to Table 1.

[6167] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM443 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6168] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 444 (VGAM444) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6169] VGAM444 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM444 was detected is described hereinabove with reference to Figs. 2-8.

[6170] VGAM444 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM444 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6171] VGAM444 gene, herein designated VGAM GENE, encodes a VGAM444 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM444 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM444 precursor RNA is designated SEQ ID:12546, and is provided hereinbelow with reference to the sequence listing part.

[6172] VGAM444 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6173] An enzyme complex designated DICER COMPLEX, dices

the VGAM444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM444 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM444 RNA is designated SEQ ID:12547, and is provided hereinbelow with reference to the sequence listing part.

[6174] VGAM444 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM444 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM444 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6175] VGAM444 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM444 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM444 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM444 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM444 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6176] The complementary binding of VGAM444 RNA, herein designated VGAM RNA, to host target binding sites on VGAM444 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM444 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM444 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6177] It is appreciated that VGAM444 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM444 host target genes. The mRNA of each one of this plurality of VGAM444 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM444 RNA, herein designated VGAM RNA, and which when bound by VGAM444 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM444 host target proteins.

[6178] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM444 gene, herein designated VGAM GENE, on one or more VGAM444 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6179] It is yet further appreciated that a function of VGAM444 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM444 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM444 correlate with, and may be deduced from, the identity of the host target genes which VGAM444 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6180] Nucleotide sequences of the VGAM444 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM444 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM444 are further described hereinbelow with reference to Table 1.

[6181] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM444 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6182] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 445 (VGAM445) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6183] VGAM445 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM445 was detected is described hereinabove with reference to Figs. 2-8.

[6184] VGAM445 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM445 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[6185] VGAM445 gene, herein designated VGAM GENE, encodes a VGAM445 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM445 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM445 precursor RNA is designated SEQ ID:12552, and is provided hereinbelow with reference to the sequence listing part.

[6186] VGAM445 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM445 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6187] An enzyme complex designated DICER COMPLEX, dices the VGAM445 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM445 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM445 RNA is designated SEQ ID:12553, and is provided hereinbelow with reference to the sequence listing part.

[6188] VGAM445 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM445 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM445 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6189] VGAM445 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM445 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM445 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM445 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM445 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6190] The complementary binding of VGAM445 RNA, herein designated VGAM RNA, to host target binding sites on VGAM445 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM445 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM445 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6191] It is appreciated that VGAM445 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM445 host target genes. The mRNA of each one of this plurality of VGAM445 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM445 RNA, herein designated VGAM RNA, and which when bound by VGAM445 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM445 host target proteins.

[6192] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM445 gene, herein designated VGAM GENE, on one or more VGAM445 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6193] It is yet further appreciated that a function of VGAM445 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM445 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM445 correlate with, and may be deduced from, the identity of the host target genes which VGAM445 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6194] Nucleotide sequences of the VGAM445 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM445 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM445 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM445 are further described hereinbelow with reference to Table 1.

[6195] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM445 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6196] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 446 (VGAM446) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6197] VGAM446 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM446 was detected is described hereinabove with reference to Figs. 2-8.

[6198] VGAM446 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM446 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[6199] VGAM446 gene, herein designated VGAM GENE, encodes a VGAM446 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM446 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM446 precursor RNA is designated SEQ ID:12568, and is provided hereinbelow with reference to the sequence listing part.

[6200] VGAM446 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6201] An enzyme complex designated DICER COMPLEX, dices the VGAM446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM446 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM446 RNA is designated SEQ ID:12569, and is provided hereinbelow with reference to the sequence listing part.

[6202] VGAM446 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM446 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM446 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6203] VGAM446 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM446 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM446 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM446 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM446 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6204] The complementary binding of VGAM446 RNA, herein designated VGAM RNA, to host target binding sites on VGAM446 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM446 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM446 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6205] It is appreciated that VGAM446 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM446 host target genes. The mRNA of each one of this plurality of VGAM446 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM446 RNA, herein designated VGAM RNA, and which when bound by VGAM446 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM446 host target proteins.

[6206] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM446 gene, herein designated VGAM GENE, on one or more VGAM446 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6207] It is yet further appreciated that a function of VGAM446 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM446 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM446 correlate with, and may be deduced from, the identity of the host target genes which VGAM446 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6208] Nucleotide sequences of the VGAM446 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM446 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM446 are further de-

scribed hereinbelow with reference to Table 1.

[6209] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM446 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6210] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 447 (VGAM447) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6211] VGAM447 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM447 was detected is described hereinabove with reference to Figs. 2-8.

[6212] VGAM447 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM447 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6213] VGAM447 gene, herein designated VGAM GENE, encodes a VGAM447 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM447 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM447 precursor RNA is designated SEQ ID:12572, and is provided hereinbelow with reference to the sequence listing part.

[6214] VGAM447 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6215] An enzyme complex designated DICER COMPLEX, dices the VGAM447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM447 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM447 RNA is designated SEQ ID:12573, and is provided hereinbelow with reference to the sequence listing part.

[6216] VGAM447 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM447 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM447 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6217] VGAM447 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM447 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM447 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM447 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM447 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6218] The complementary binding of VGAM447 RNA, herein designated VGAM RNA, to host target binding sites on VGAM447 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM447 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM447 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6219] It is appreciated that VGAM447 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM447 host target genes. The mRNA of each one of this plurality of VGAM447 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM447 RNA, herein designated VGAM RNA, and which when bound by VGAM447 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM447 host target proteins.

[6220] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM447 gene, herein designated VGAM GENE, on one or more VGAM447 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6221] It is yet further appreciated that a function of VGAM447 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM447 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM447 correlate with, and may be deduced from, the identity of the host target genes which VGAM447 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6222] Nucleotide sequences of the VGAM447 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM447 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM447 are further described hereinbelow with reference to Table 1.

[6223] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM447 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6224] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 448 (VGAM448) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6225] VGAM448 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM448 was detected is described hereinabove with reference to Figs. 2-8.

[6226] VGAM448 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM448 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6227] VGAM448 gene, herein designated VGAM GENE, encodes a

VGAM448 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM448 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM448 precursor RNA is designated SEQ ID:12575, and is provided hereinbelow with reference to the sequence listing part.

[6228] VGAM448 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6229] An enzyme complex designated DICER COMPLEX, dices the VGAM448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM448 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM448 RNA is designated SEQ ID:12576, and is provided hereinbelow with reference to the sequence listing part.

[6230] VGAM448 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM448 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM448 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6231] VGAM448 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM448 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM448 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM448 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM448 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6232] The complementary binding of VGAM448 RNA, herein designated VGAM RNA, to host target binding sites on VGAM448 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM448 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM448 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[6233] It is appreciated that VGAM448 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM448 host target genes. The mRNA of each one of this plurality of VGAM448 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM448 RNA, herein designated VGAM RNA, and which when bound by VGAM448 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM448 host target proteins.

[6234] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM448 gene, herein designated VGAM GENE, on one or more VGAM448 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6235] It is yet further appreciated that a function of VGAM448 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM448 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM448 correlate with, and may be deduced from, the identity of the host target genes which VGAM448 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6236] Nucleotide sequences of the VGAM448 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM448 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM448 are further described hereinbelow with reference to Table 1.

[6237] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM448 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6238] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 449 (VGAM449) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6239] VGAM449 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM449 was detected is described hereinabove with reference to Figs. 2-8.

[6240] VGAM449 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM449 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6241] VGAM449 gene, herein designated VGAM GENE, encodes a VGAM449 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM449 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM449 precursor RNA is designated SEQ ID:12592, and is provided hereinbelow with reference to the sequence listing part.

[6242] VGAM449 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6243] An enzyme complex designated DICER COMPLEX, dices the VGAM449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM449 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM449 RNA is designated SEQ ID:12593, and is provided hereinbelow with reference to the sequence listing part.

[6244] VGAM449 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM449 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM449 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6245] VGAM449 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM449 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM449 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM449 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM449 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6246] The complementary binding of VGAM449 RNA, herein designated VGAM RNA, to host target binding sites on VGAM449 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM449 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM449 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6247] It is appreciated that VGAM449 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM449 host target genes. The mRNA of each one of this plurality of VGAM449 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM449 RNA, herein designated VGAM RNA, and which when bound by VGAM449 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM449 host target proteins.

[6248] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM449 gene, herein designated VGAM GENE, on one or more VGAM449 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6249] It is yet further appreciated that a function of VGAM449 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM449 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM449 correlate with, and may be deduced from, the identity of the host target genes which VGAM449 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6250] Nucleotide sequences of the VGAM449 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM449 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM449 are further described hereinbelow with reference to Table 1.

[6251] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM449 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6252] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 450 (VGAM450) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6253] VGAM450 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM450 was detected is described hereinabove with reference to Figs. 2–8.

[6254] VGAM450 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM450 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6255] VGAM450 gene, herein designated VGAM GENE, encodes a VGAM450 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM450 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM450 precursor RNA is designated SEQ ID:12713, and is provided hereinbelow with reference to the sequence listing part.

[6256] VGAM450 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6257] An enzyme complex designated DICER COMPLEX, dices the VGAM450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM450 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM450 RNA is designated SEQ ID:12714, and is provided hereinbelow with reference to the sequence listing part.

[6258] VGAM450 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM450 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM450 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6259] VGAM450 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM450 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM450 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM450 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM450 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6260] The complementary binding of VGAM450 RNA, herein designated VGAM RNA, to host target binding sites on VGAM450 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM450 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM450 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6261] It is appreciated that VGAM450 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM450 host target genes. The mRNA of each one of this plurality of VGAM450 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM450 RNA, herein designated VGAM RNA, and which when bound by VGAM450 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM450 host target proteins.

[6262] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM450 gene, herein designated VGAM GENE, on one or more VGAM450 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6263] It is yet further appreciated that a function of VGAM450 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM450 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM450 correlate with, and may be deduced from, the identity of the host target genes which VGAM450 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6264] Nucleotide sequences of the VGAM450 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM450 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM450 are further described hereinbelow with reference to Table 1.

[6265] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM450 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6266] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 451 (VGAM451) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6267] VGAM451 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM451 was detected is described hereinabove with reference to Figs. 2–8.

[6268] VGAM451 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM451 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6269] VGAM451 gene, herein designated VGAM GENE, encodes a VGAM451 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM451 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM451 precursor RNA is designated SEQ ID:12718, and is provided hereinbelow with reference to the sequence listing part.

[6270] VGAM451 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM451 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6271] An enzyme complex designated DICER COMPLEX, dices the VGAM451 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM451 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 55%) nucleotide sequence of VGAM451 RNA is designated SEQ ID:12719, and is provided hereinbelow with reference to the sequence listing part.

[6272] VGAM451 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM451 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM451 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6273] VGAM451 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM451 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM451 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM451 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM451 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6274] The complementary binding of VGAM451 RNA, herein designated VGAM RNA, to host target binding sites on VGAM451 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM451 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM451 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6275] It is appreciated that VGAM451 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM451 host target genes. The mRNA of each one of this plurality of VGAM451 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM451 RNA, herein designated VGAM RNA, and which when bound by VGAM451 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM451 host target proteins.

[6276] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM451 gene, herein designated VGAM GENE, on one or more VGAM451 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[6277] It is yet further appreciated that a function of VGAM451 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM451 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM451 correlate with, and may be deduced from, the identity of the host target genes which VGAM451 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6278] Nucleotide sequences of the VGAM451 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM451 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM451 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM451 are further described hereinbelow with reference to Table 1.

[6279] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM451 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6280] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 452 (VGAM452) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6281] VGAM452 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM452 was detected is described hereinabove with reference to Figs. 2–8.

[6282] VGAM452 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM452 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6283] VGAM452 gene, herein designated VGAM GENE, encodes a VGAM452 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM452 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM452 precursor RNA is designated SEQ ID:12734, and is provided hereinbelow with reference to the sequence listing part.

[6284] VGAM452 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM452 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6285] An enzyme complex designated DICER COMPLEX, dices the VGAM452 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM452 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM452 RNA is designated SEQ ID:12735, and is provided hereinbelow with reference to the sequence listing part.

[6286] VGAM452 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM452 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM452 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6287] VGAM452 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM452 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM452 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM452 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM452 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6288] The complementary binding of VGAM452 RNA, herein designated VGAM RNA, to host target binding sites on VGAM452 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM452 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM452 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6289] It is appreciated that VGAM452 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM452 host target genes. The mRNA of

each one of this plurality of VGAM452 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM452 RNA, herein designated VGAM RNA, and which when bound by VGAM452 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM452 host target proteins.

[6290] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM452 gene, herein designated VGAM GENE, on one or more VGAM452 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[6291] It is yet further appreciated that a function of VGAM452 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM452 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM452 correlate with, and may be deduced from, the identity of the host target genes which VGAM452 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6292] Nucleotide sequences of the VGAM452 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM452 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM452 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM452 are further described hereinbelow with reference to Table 1.

[6293] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM452 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[6294] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 453 (VGAM453) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6295] VGAM453 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM453 was detected is described hereinabove with reference to Figs. 2–8.

[6296] VGAM453 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM453 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6297] VGAM453 gene, herein designated VGAM GENE, encodes a VGAM453 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM453 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar



to the nucleotide sequence of VGAM453 precursor RNA is designated SEQ ID:12751, and is provided hereinbelow with reference to the sequence listing part.

[6298] VGAM453 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6299] An enzyme complex designated DICER COMPLEX, dices the VGAM453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM453 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM453 RNA is designated SEQ ID:12752, and

is provided hereinbelow with reference to the sequence listing part.

[6300] VGAM453 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM453 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM453 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6301] VGAM453 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM453 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM453 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM453 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM453 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6302] The complementary binding of VGAM453 RNA, herein designated VGAM RNA, to host target binding sites on VGAM453 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM453 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM453 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6303] It is appreciated that VGAM453 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM453 host target genes. The mRNA of each one of this plurality of VGAM453 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM453 RNA, herein designated VGAM RNA, and which when bound by VGAM453 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM453 host target proteins.

[6304] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM453 gene, herein designated VGAM GENE, on one or more VGAM453 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6305] It is yet further appreciated that a function of VGAM453 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM453 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM453 correlate with, and may be deduced from, the identity of the host target genes which VGAM453 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6306] Nucleotide sequences of the VGAM453 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM453 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM453 are further described hereinbelow with reference to Table 1.

[6307] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM453 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6308] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 454 (VGAM454) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6309] VGAM454 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM454 was detected is described hereinabove with reference to Figs. 2–8.

[6310] VGAM454 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM454 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6311] VGAM454 gene, herein designated VGAM GENE, encodes a VGAM454 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM454 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM454 precursor RNA is

designated SEQ ID:12765, and is provided hereinbelow with reference to the sequence listing part.

[6312] VGAM454 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM454 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6313] An enzyme complex designated DICER COMPLEX, dices the VGAM454 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM454 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM454 RNA is designated SEQ ID:12766, and is provided hereinbelow with reference to the sequence

listing part.

[6314] VGAM454 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM454 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM454 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6315] VGAM454 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM454 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM454 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM454 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM454 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6316] The complementary binding of VGAM454 RNA, herein designated VGAM RNA, to host target binding sites on VGAM454 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM454 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM454 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6317] It is appreciated that VGAM454 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM454 host target genes. The mRNA of each one of this plurality of VGAM454 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM454 RNA, herein designated VGAM RNA, and which when bound by VGAM454 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM454 host target proteins.

[6318] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM454 gene, herein designated VGAM GENE, on one or more VGAM454 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6319] It is yet further appreciated that a function of VGAM454 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM454 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM454 correlate with, and may be deduced from, the identity of the host target genes which VGAM454 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6320] Nucleotide sequences of the VGAM454 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM454 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM454 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM454 are further described hereinbelow with reference to Table 1.

[6321] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM454 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6322] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 455 (VGAM455) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6323] VGAM455 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM455 was detected is described hereinabove with reference to Figs. 2–8.

[6324] VGAM455 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM455 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6325] VGAM455 gene, herein designated VGAM GENE, encodes a VGAM455 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM455 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM455 precursor RNA is designated SEQ ID:12797, and is provided hereinbelow

with reference to the sequence listing part.

[6326] VGAM455 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6327] An enzyme complex designated DICER COMPLEX, dices the VGAM455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM455 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM455 RNA is designated SEQ ID:12798, and is provided hereinbelow with reference to the sequence listing part.

[6328] VGAM455 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM455 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM455 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6329] VGAM455 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM455 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM455 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM455 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM455 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6330] The complementary binding of VGAM455 RNA, herein designated VGAM RNA, to host target binding sites on VGAM455 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM455 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM455 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6331] It is appreciated that VGAM455 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM455 host target genes. The mRNA of each one of this plurality of VGAM455 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM455 RNA, herein designated VGAM RNA, and which when bound by VGAM455 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM455 host target proteins.

[6332] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM455 gene, herein designated VGAM GENE, on one or more VGAM455 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6333] It is yet further appreciated that a function of VGAM455 is inhibition of expression of host target genes, as part of a



novel viral mechanism of attacking a host. Accordingly, utilities of VGAM455 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM455 correlate with, and may be deduced from, the identity of the host target genes which VGAM455 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6334] Nucleotide sequences of the VGAM455 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM455 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM455 are further described hereinbelow with reference to Table 1.

[6335] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM455 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6336] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 456 (VGAM456) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6337] VGAM456 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM456 was detected is described hereinabove with reference to Figs. 2–8.

[6338] VGAM456 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM456 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6339] VGAM456 gene, herein designated VGAM GENE, encodes a VGAM456 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM456 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM456 precursor RNA is designated SEQ ID:12800, and is provided hereinbelow with reference to the sequence listing part.

[6340] VGAM456 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM456 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6341] An enzyme complex designated DICER COMPLEX, dices the VGAM456 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM456 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM456 RNA is designated SEQ ID:12801, and is provided hereinbelow with reference to the sequence listing part.

[6342] VGAM456 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM456 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM456 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6343] VGAM456 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM456 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM456 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM456 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM456 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6344] The complementary binding of VGAM456 RNA, herein designated VGAM RNA, to host target binding sites on VGAM456 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM456 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM456 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6345] It is appreciated that VGAM456 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM456 host target genes. The mRNA of each one of this plurality of VGAM456 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM456 RNA, herein designated VGAM

RNA, and which when bound by VGAM456 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM456 host target proteins.

[6346] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM456 gene, herein designated VGAM GENE, on one or more VGAM456 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6347] It is yet further appreciated that a function of VGAM456 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM456 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM456 correlate with, and may be deduced from, the identity of the host target genes which VGAM456 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6348] Nucleotide sequences of the VGAM456 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM456 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM456 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM456 are further described hereinbelow with reference to Table 1.

[6349] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM456 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6350] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 457 (VGAM457) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6351] VGAM457 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM457 was detected is described hereinabove with reference to Figs. 2–8.

[6352] VGAM457 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM457 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6353] VGAM457 gene, herein designated VGAM GENE, encodes a VGAM457 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM457 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM457 precursor RNA is designated SEQ ID:12806, and is provided hereinbelow with reference to the sequence listing part.

[6354] VGAM457 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM457 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6355] An enzyme complex designated DICER COMPLEX, dices the VGAM457 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM457 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM457 RNA is designated SEQ ID:12807, and is provided hereinbelow with reference to the sequence listing part.

[6356] VGAM457 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM457 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM457 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6357] VGAM457 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM457 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM457 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM457 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM457 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6358] The complementary binding of VGAM457 RNA, herein designated VGAM RNA, to host target binding sites on VGAM457 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM457 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM457 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6359] It is appreciated that VGAM457 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM457 host target genes. The mRNA of each one of this plurality of VGAM457 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM457 RNA, herein designated VGAM RNA, and which when bound by VGAM457 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM457 host target proteins.

[6360] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM457 gene, herein designated VGAM GENE, on one or more VGAM457 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6361] It is yet further appreciated that a function of VGAM457 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM457 include diagnosis, prevention and

treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM457 correlate with, and may be deduced from, the identity of the host target genes which VGAM457 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6362] Nucleotide sequences of the VGAM457 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM457 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM457 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM457 are further described hereinbelow with reference to Table 1.

[6363] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM457 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6364] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 458 (VGAM458) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6365] VGAM458 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM458 was detected is described hereinabove with reference to Figs. 2–8.

[6366] VGAM458 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM458 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6367] VGAM458 gene, herein designated VGAM GENE, encodes a VGAM458 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM458 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM458 precursor RNA is designated SEQ ID:12822, and is provided hereinbelow with reference to the sequence listing part.

[6368] VGAM458 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM458 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6369] An enzyme complex designated DICER COMPLEX, dices the VGAM458 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM458 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM458 RNA is designated SEQ ID:12823, and is provided hereinbelow with reference to the sequence listing part.

[6370] VGAM458 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM458 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM458 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6371] VGAM458 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM458 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM458 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM458 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM458 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6372] The complementary binding of VGAM458 RNA, herein designated VGAM RNA, to host target binding sites on VGAM458 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM458 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM458 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6373] It is appreciated that VGAM458 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM458 host target genes. The mRNA of each one of this plurality of VGAM458 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM458 RNA, herein designated VGAM RNA, and which when bound by VGAM458 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM458 host target proteins.

[6374] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM458 gene, herein designated VGAM GENE, on one or more VGAM458 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6375] It is yet further appreciated that a function of VGAM458 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM458 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific

functions, and accordingly utilities, of VGAM458 correlate with, and may be deduced from, the identity of the host target genes which VGAM458 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6376] Nucleotide sequences of the VGAM458 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM458 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM458 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM458 are further described hereinbelow with reference to Table 1.

[6377] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM458 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6378] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 459 (VGAM459) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[6379] VGAM459 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM459 was detected is described hereinabove with reference to Figs. 2–8.

[6380] VGAM459 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine foamy virus. VGAM459 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6381] VGAM459 gene, herein designated VGAM GENE, encodes a VGAM459 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM459 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM459 precursor RNA is designated SEQ ID:12830, and is provided hereinbelow with reference to the sequence listing part.

[6382] VGAM459 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM459 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6383] An enzyme complex designated DICER COMPLEX, dices the VGAM459 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM459 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM459 RNA is designated SEQ ID:12831, and is provided hereinbelow with reference to the sequence listing part.

[6384] VGAM459 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM459 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM459 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6385] VGAM459 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM459 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM459 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM459 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM459 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6386] The complementary binding of VGAM459 RNA, herein designated VGAM RNA, to host target binding sites on VGAM459 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM459 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM459 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6387] It is appreciated that VGAM459 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM459 host target genes. The mRNA of each one of this plurality of VGAM459 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM459 RNA, herein designated VGAM RNA, and which when bound by VGAM459 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM459 host target proteins.

[6388] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM459 gene, herein designated VGAM GENE, on one or more VGAM459 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6389] It is yet further appreciated that a function of VGAM459 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM459 include diagnosis, prevention and treatment of viral infection by Equine foamy virus. Specific functions, and accordingly utilities, of VGAM459 correlate



with, and may be deduced from, the identity of the host target genes which VGAM459 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6390] Nucleotide sequences of the VGAM459 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM459 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM459 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM459 are further described hereinbelow with reference to Table 1.

[6391] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM459 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6392] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 460 (VGAM460) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[6393] VGAM460 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM460 was detected is described hereinabove with reference to Figs. 2–8.

[6394] VGAM460 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine adenovirus. VGAM460 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6395] VGAM460 gene, herein designated VGAM GENE, encodes a VGAM460 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM460 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM460 precursor RNA is designated SEQ ID:12845, and is provided hereinbelow with reference to the sequence listing part.

[6396] VGAM460 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6397] An enzyme complex designated DICER COMPLEX, dices the VGAM460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM460 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM460 RNA is designated SEQ ID:12846, and is provided hereinbelow with reference to the sequence listing part.

[6398] VGAM460 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM460 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM460 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6399] VGAM460 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM460 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM460 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM460 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM460 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6400] The complementary binding of VGAM460 RNA, herein designated VGAM RNA, to host target binding sites on VGAM460 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM460 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM460 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6401] It is appreciated that VGAM460 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM460 host target genes. The mRNA of each one of this plurality of VGAM460 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM460 RNA, herein designated VGAM RNA, and which when bound by VGAM460 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM460 host target proteins.

[6402] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM460 gene, herein designated VGAM GENE, on one or more VGAM460 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6403] It is yet further appreciated that a function of VGAM460 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM460 include diagnosis, prevention and treatment of viral infection by Canine adenovirus. Specific functions, and accordingly utilities, of VGAM460 correlate with, and may be deduced from, the identity of the host

target genes which VGAM460 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6404] Nucleotide sequences of the VGAM460 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM460 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM460 are further described hereinbelow with reference to Table 1.

[6405] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM460 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6406] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 461 (VGAM461) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6407] VGAM461 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM461 was detected is described hereinabove with reference to Figs. 2–8.

[6408] VGAM461 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine foamy virus. VGAM461 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6409] VGAM461 gene, herein designated VGAM GENE, encodes a VGAM461 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM461 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM461 precursor RNA is designated SEQ ID:12850, and is provided hereinbelow with reference to the sequence listing part.

[6410] VGAM461 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6411] An enzyme complex designated DICER COMPLEX, dices the VGAM461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM461 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM461 RNA is designated SEQ ID:12851, and is provided hereinbelow with reference to the sequence listing part.

[6412] VGAM461 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM461 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM461 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6413] VGAM461 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM461 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM461 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM461 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM461 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6414] The complementary binding of VGAM461 RNA, herein designated VGAM RNA, to host target binding sites on VGAM461 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM461 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM461 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6415] It is appreciated that VGAM461 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM461 host target genes. The mRNA of each one of this plurality of VGAM461 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM461 RNA, herein designated VGAM RNA, and which when bound by VGAM461 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM461 host target proteins.

[6416] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM461 gene, herein designated VGAM GENE, on one or more VGAM461 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6417] It is yet further appreciated that a function of VGAM461 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM461 include diagnosis, prevention and treatment of viral infection by Equine foamy virus. Specific functions, and accordingly utilities, of VGAM461 correlate with, and may be deduced from, the identity of the host target genes which VGAM461 binds and inhibits, and the

function of these host target genes, as elaborated herein—below.

[6418] Nucleotide sequences of the VGAM461 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM461 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM461 are further described hereinbelow with reference to Table 1.

[6419] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM461 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6420] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 462 (VGAM462) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6421] VGAM462 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM462 was detected is described hereinabove with reference to Figs. 2–8.

[6422] VGAM462 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine foamy virus. VGAM462 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6423] VGAM462 gene, herein designated VGAM GENE, encodes a VGAM462 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM462 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM462 precursor RNA is designated SEQ ID:12857, and is provided hereinbelow with reference to the sequence listing part.

[6424] VGAM462 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM462 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6425] An enzyme complex designated DICER COMPLEX, dices the VGAM462 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM462 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM462 RNA is designated SEQ ID:12858, and is provided hereinbelow with reference to the sequence listing part.

[6426] VGAM462 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM462 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM462 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6427] VGAM462 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM462 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM462 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM462 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM462 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[6428] The complementary binding of VGAM462 RNA, herein designated VGAM RNA, to host target binding sites on VGAM462 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM462 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM462 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6429] It is appreciated that VGAM462 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM462 host target genes. The mRNA of each one of this plurality of VGAM462 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM462 RNA, herein designated VGAM RNA, and which when bound by VGAM462 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM462 host target proteins.

[6430] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM462 gene, herein designated VGAM GENE, on one or more VGAM462 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6431] It is yet further appreciated that a function of VGAM462 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM462 include diagnosis, prevention and treatment of viral infection by Equine foamy virus. Specific functions, and accordingly utilities, of VGAM462 correlate with, and may be deduced from, the identity of the host target genes which VGAM462 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[6432] Nucleotide sequences of the VGAM462 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM462 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM462 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM462 are further described hereinbelow with reference to Table 1.

[6433] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM462 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6434] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 463 (VGAM463) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6435] VGAM463 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM463 was detected is described hereinabove with reference to Figs. 2–8.

[6436] VGAM463 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine foamy virus.

VGAM463 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6437] VGAM463 gene, herein designated VGAM GENE, encodes a VGAM463 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM463 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM463 precursor RNA is designated SEQ ID:12880, and is provided hereinbelow with reference to the sequence listing part.

[6438] VGAM463 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6439] An enzyme complex designated DICER COMPLEX, dices the VGAM463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM463 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM463 RNA is designated SEQ ID:12881, and is provided hereinbelow with reference to the sequence listing part.

[6440] VGAM463 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM463 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM463 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[6441] VGAM463 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM463 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM463 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM463 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM463 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6442] The complementary binding of VGAM463 RNA, herein designated VGAM RNA, to host target binding sites on VGAM463 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM463 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM463 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6443] It is appreciated that VGAM463 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM463 host target genes. The mRNA of each one of this plurality of VGAM463 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM463 RNA, herein designated VGAM RNA, and which when bound by VGAM463 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM463 host target proteins.

[6444] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM463 gene, herein designated VGAM GENE, on one or

more VGAM463 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6445] It is yet further appreciated that a function of VGAM463 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM463 include diagnosis, prevention and treatment of viral infection by Equine foamy virus. Specific functions, and accordingly utilities, of VGAM463 correlate with, and may be deduced from, the identity of the host target genes which VGAM463 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[6446] Nucleotide sequences of the VGAM463 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM463 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM463 are further described hereinbelow with reference to Table 1.

[6447] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM463 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6448] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 464 (VGAM464) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6449] VGAM464 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM464 was detected is described

hereinabove with reference to Figs. 2–8.

[6450] VGAM464 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine adenovirus.

VGAM464 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6451] VGAM464 gene, herein designated VGAM GENE, encodes a VGAM464 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM464 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM464 precursor RNA is designated SEQ ID:12890, and is provided hereinbelow with reference to the sequence listing part.

[6452] VGAM464 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6453] An enzyme complex designated DICER COMPLEX, dices the VGAM464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM464 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM464 RNA is designated SEQ ID:12891, and is provided hereinbelow with reference to the sequence listing part.

[6454] VGAM464 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM464 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM464 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6455] VGAM464 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM464 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM464 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM464 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM464 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6456] The complementary binding of VGAM464 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM464 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM464 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM464 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6457] It is appreciated that VGAM464 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM464 host target genes. The mRNA of each one of this plurality of VGAM464 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM464 RNA, herein designated VGAM RNA, and which when bound by VGAM464 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM464 host target proteins.

[6458] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM464 gene, herein designated VGAM GENE, on one or more VGAM464 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6459] It is yet further appreciated that a function of VGAM464 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM464 include diagnosis, prevention and treatment of viral infection by Canine adenovirus. Specific functions, and accordingly utilities, of VGAM464 correlate with, and may be deduced from, the identity of the host target genes which VGAM464 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6460] Nucleotide sequences of the VGAM464 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM464 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM464 are further described hereinbelow with reference to Table 1.

[6461] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM464 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6462] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 465 (VGAM465) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6463] VGAM465 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM465 was detected is described hereinabove with reference to Figs. 2-8.

[6464] VGAM465 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM465 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6465] VGAM465 gene, herein designated VGAM GENE, encodes a VGAM465 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM465 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM465 precursor RNA is designated SEQ ID:12917, and is provided hereinbelow with reference to the sequence listing part.

[6466] VGAM465 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[6467] An enzyme complex designated DICER COMPLEX, dices the VGAM465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM465 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM465 RNA is designated SEQ ID:12918, and is provided hereinbelow with reference to the sequence listing part.

[6468] VGAM465 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM465 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM465 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6469] VGAM465 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM465 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM465 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM465 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM465 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6470] The complementary binding of VGAM465 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM465 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM465 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM465 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6471] It is appreciated that VGAM465 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM465 host target genes. The mRNA of each one of this plurality of VGAM465 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM465 RNA, herein designated VGAM RNA, and which when bound by VGAM465 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM465 host target proteins.

[6472] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM465 gene, herein designated VGAM GENE, on one or more VGAM465 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6473] It is yet further appreciated that a function of VGAM465 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM465 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM465 correlate with, and may be deduced from, the identity of the host target genes which VGAM465 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6474] Nucleotide sequences of the VGAM465 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM465 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM465 are further described hereinbelow with reference to Table 1.

[6475] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM465 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6476] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 466 (VGAM466) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6477] VGAM466 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM466 was detected is described hereinabove with reference to Figs. 2-8.

[6478] VGAM466 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human adenovirus E. VGAM466 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6479] VGAM466 gene, herein designated VGAM GENE, encodes a VGAM466 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM466 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM466 precursor RNA is designated SEQ ID:12952, and is provided hereinbelow with reference to the sequence listing part.

[6480] VGAM466 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6481] An enzyme complex designated DICER COMPLEX, dices the VGAM466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM466 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM466 RNA is designated SEQ ID:12953, and is provided hereinbelow with reference to the sequence listing part.

[6482] VGAM466 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM466 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM466 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6483] VGAM466 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM466 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM466 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM466 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM466 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6484] The complementary binding of VGAM466 RNA, herein designated VGAM RNA, to host target binding sites on VGAM466 host target RNA, herein designated VGAM HOST



TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM466 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM466 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6485] It is appreciated that VGAM466 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM466 host target genes. The mRNA of each one of this plurality of VGAM466 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM466 RNA, herein designated VGAM RNA, and which when bound by VGAM466 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM466 host target proteins.

[6486] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM466 gene, herein designated VGAM GENE, on one or more VGAM466 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6487] It is yet further appreciated that a function of VGAM466 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM466 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM466 correlate with, and may be deduced from, the identity of the host target genes which VGAM466 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6488] Nucleotide sequences of the VGAM466 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM466 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM466 are further described hereinbelow with reference to Table 1.

[6489] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM466 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6490] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 467 (VGAM467) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6491] VGAM467 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM467 was detected is described hereinabove with reference to Figs. 2-8.

[6492] VGAM467 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5.

VGAM467 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6493] VGAM467 gene, herein designated VGAM GENE, encodes a VGAM467 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM467 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM467 precursor RNA is designated SEQ ID:12981, and is provided hereinbelow with reference to the sequence listing part.

[6494] VGAM467 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6495] An enzyme complex designated DICER COMPLEX, dices

the VGAM467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM467 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM467 RNA is designated SEQ ID:12982, and is provided hereinbelow with reference to the sequence listing part.

[6496] VGAM467 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM467 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM467 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6497] VGAM467 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM467 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM467 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM467 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM467 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6498] The complementary binding of VGAM467 RNA, herein designated VGAM RNA, to host target binding sites on VGAM467 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM467 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM467 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6499] It is appreciated that VGAM467 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM467 host target genes. The mRNA of each one of this plurality of VGAM467 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM467 RNA, herein designated VGAM RNA, and which when bound by VGAM467 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM467 host target proteins.

[6500] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM467 gene, herein designated VGAM GENE, on one or more VGAM467 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6501] It is yet further appreciated that a function of VGAM467 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM467 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM467 correlate with, and may be deduced from, the identity of the host target genes which VGAM467 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6502] Nucleotide sequences of the VGAM467 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM467 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM467 are further described hereinbelow with reference to Table 1.

[6503] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM467 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6504] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 468 (VGAM468) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6505] VGAM468 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM468 was detected is described hereinabove with reference to Figs. 2-8.

[6506] VGAM468 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Planococcus citri densovirus. VGAM468 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6507] VGAM468 gene, herein designated VGAM GENE, encodes a VGAM468 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM468 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM468 precursor RNA is designated SEQ ID:12987, and is provided hereinbelow with reference to the sequence listing part.

[6508] VGAM468 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM468 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6509] An enzyme complex designated DICER COMPLEX, dices the VGAM468 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM468 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM468 RNA is designated SEQ ID:12988, and is provided hereinbelow with reference to the sequence listing part.

[6510] VGAM468 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM468 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM468 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6511] VGAM468 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM468 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM468 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM468 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM468 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6512] The complementary binding of VGAM468 RNA, herein designated VGAM RNA, to host target binding sites on VGAM468 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM468 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM468 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6513] It is appreciated that VGAM468 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM468 host target genes. The mRNA of each one of this plurality of VGAM468 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM468 RNA, herein designated VGAM RNA, and which when bound by VGAM468 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM468 host target proteins.

[6514] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM468 gene, herein designated VGAM GENE, on one or more VGAM468 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6515] It is yet further appreciated that a function of VGAM468 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM468 include diagnosis, prevention and treatment of viral infection by Planococcus citri densovirus. Specific functions, and accordingly utilities, of VGAM468 correlate with, and may be deduced from, the identity of the host target genes which VGAM468 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6516] Nucleotide sequences of the VGAM468 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM468 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM468 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM468 are further described hereinbelow with reference to Table 1.

[6517] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM468 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6518] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 469 (VGAM469) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6519] VGAM469 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM469 was detected is described hereinabove with reference to Figs. 2-8.

[6520] VGAM469 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Planococcus citri densovirus. VGAM469 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[6521] VGAM469 gene, herein designated VGAM GENE, encodes a VGAM469 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM469 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM469 precursor RNA is designated SEQ ID:12998, and is provided hereinbelow with reference to the sequence listing part.

[6522] VGAM469 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM469 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6523] An enzyme complex designated DICER COMPLEX, dices the VGAM469 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM469 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM469 RNA is designated SEQ ID:12999, and is provided hereinbelow with reference to the sequence listing part.

[6524] VGAM469 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM469 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM469 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6525] VGAM469 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM469 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM469 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM469 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM469 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6526] The complementary binding of VGAM469 RNA, herein designated VGAM RNA, to host target binding sites on VGAM469 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM469 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM469 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6527] It is appreciated that VGAM469 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM469 host target genes. The mRNA of each one of this plurality of VGAM469 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM469 RNA, herein designated VGAM RNA, and which when bound by VGAM469 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM469 host target proteins.

[6528] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM469 gene, herein designated VGAM GENE, on one or more VGAM469 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6529] It is yet further appreciated that a function of VGAM469 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM469 include diagnosis, prevention and treatment of viral infection by Planococcus citri densovirus. Specific functions, and accordingly utilities, of VGAM469 correlate with, and may be deduced from, the identity of the host target genes which VGAM469 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6530] Nucleotide sequences of the VGAM469 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM469 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM469 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM469 are further de-

scribed hereinbelow with reference to Table 1.

[6531] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM469 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6532] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 470 (VGAM470) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6533] VGAM470 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM470 was detected is described hereinabove with reference to Figs. 2-8.

[6534] VGAM470 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Planococcus citri densovirus. VGAM470 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6535] VGAM470 gene, herein designated VGAM GENE, encodes a VGAM470 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM470 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM470 precursor RNA is designated SEQ ID:13006, and is provided hereinbelow with reference to the sequence listing part.

[6536] VGAM470 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6537] An enzyme complex designated DICER COMPLEX, dices the VGAM470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM470 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM470 RNA is designated SEQ ID:13007, and is provided hereinbelow with reference to the sequence listing part.

[6538] VGAM470 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM470 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM470 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6539] VGAM470 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM470 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM470 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM470 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM470 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6540] The complementary binding of VGAM470 RNA, herein designated VGAM RNA, to host target binding sites on VGAM470 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM470 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM470 host target protein, herein designated



VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6541] It is appreciated that VGAM470 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM470 host target genes. The mRNA of each one of this plurality of VGAM470 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM470 RNA, herein designated VGAM RNA, and which when bound by VGAM470 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM470 host target proteins.

[6542] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM470 gene, herein designated VGAM GENE, on one or more VGAM470 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6543] It is yet further appreciated that a function of VGAM470 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM470 include diagnosis, prevention and treatment of viral infection by Planococcus citri densovirus. Specific functions, and accordingly utilities, of VGAM470 correlate with, and may be deduced from, the identity of the host target genes which VGAM470 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6544] Nucleotide sequences of the VGAM470 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM470 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM470 are further described hereinbelow with reference to Table 1.

[6545] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM470 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6546] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 471 (VGAM471) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6547] VGAM471 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM471 was detected is described hereinabove with reference to Figs. 2-8.

[6548] VGAM471 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Zaire Ebola virus. VGAM471 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6549] VGAM471 gene, herein designated VGAM GENE, encodes a

VGAM471 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM471 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM471 precursor RNA is designated SEQ ID:13041, and is provided hereinbelow with reference to the sequence listing part.

[6550] VGAM471 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6551] An enzyme complex designated DICER COMPLEX, dices the VGAM471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM471 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM471 RNA is designated SEQ ID:13042, and is provided hereinbelow with reference to the sequence listing part.

[6552] VGAM471 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM471 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM471 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6553] VGAM471 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM471 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM471 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM471 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM471 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6554] The complementary binding of VGAM471 RNA, herein designated VGAM RNA, to host target binding sites on VGAM471 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM471 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM471 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[6555] It is appreciated that VGAM471 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM471 host target genes. The mRNA of each one of this plurality of VGAM471 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM471 RNA, herein designated VGAM RNA, and which when bound by VGAM471 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM471 host target proteins.

[6556] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM471 gene, herein designated VGAM GENE, on one or more VGAM471 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6557] It is yet further appreciated that a function of VGAM471 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM471 include diagnosis, prevention and treatment of viral infection by Zaire Ebola virus. Specific functions, and accordingly utilities, of VGAM471 correlate with, and may be deduced from, the identity of the host target genes which VGAM471 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6558] Nucleotide sequences of the VGAM471 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM471 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM471 are further described hereinbelow with reference to Table 1.

[6559] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM471 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6560] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 472 (VGAM472) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6561] VGAM472 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM472 was detected is described hereinabove with reference to Figs. 2-8.

[6562] VGAM472 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Planococcus citri densovirus. VGAM472 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6563] VGAM472 gene, herein designated VGAM GENE, encodes a VGAM472 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM472 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM472 precursor RNA is designated SEQ ID:13051, and is provided hereinbelow with reference to the sequence listing part.

[6564] VGAM472 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6565] An enzyme complex designated DICER COMPLEX, dices the VGAM472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM472 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM472 RNA is designated SEQ ID:13052, and is provided hereinbelow with reference to the sequence listing part.

[6566] VGAM472 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM472 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM472 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6567] VGAM472 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM472 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM472 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM472 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM472 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6568] The complementary binding of VGAM472 RNA, herein designated VGAM RNA, to host target binding sites on VGAM472 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM472 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM472 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6569] It is appreciated that VGAM472 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM472 host target genes. The mRNA of each one of this plurality of VGAM472 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM472 RNA, herein designated VGAM RNA, and which when bound by VGAM472 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM472 host target proteins.

[6570] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM472 gene, herein designated VGAM GENE, on one or more VGAM472 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6571] It is yet further appreciated that a function of VGAM472 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM472 include diagnosis, prevention and treatment of viral infection by Planococcus citri denso-virus. Specific functions, and accordingly utilities, of VGAM472 correlate with, and may be deduced from, the identity of the host target genes which VGAM472 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6572] Nucleotide sequences of the VGAM472 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM472 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM472 are further described hereinbelow with reference to Table 1.

[6573] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM472 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6574] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 473 (VGAM473) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6575] VGAM473 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM473 was detected is described hereinabove with reference to Figs. 2–8.

[6576] VGAM473 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Acyrthosiphon pisum virus. VGAM473 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6577] VGAM473 gene, herein designated VGAM GENE, encodes a VGAM473 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM473 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM473 precursor RNA is designated SEQ ID:13068, and is provided hereinbelow with reference to the sequence listing part.

[6578] VGAM473 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6579] An enzyme complex designated DICER COMPLEX, dices the VGAM473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM473 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM473 RNA is designated SEQ ID:13069, and is provided hereinbelow with reference to the sequence listing part.

[6580] VGAM473 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM473 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM473 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6581] VGAM473 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM473 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM473 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM473 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM473 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6582] The complementary binding of VGAM473 RNA, herein designated VGAM RNA, to host target binding sites on VGAM473 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM473 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM473 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6583] It is appreciated that VGAM473 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM473 host target genes. The mRNA of each one of this plurality of VGAM473 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM473 RNA, herein designated VGAM RNA, and which when bound by VGAM473 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM473 host target proteins.

[6584] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM473 gene, herein designated VGAM GENE, on one or more VGAM473 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6585] It is yet further appreciated that a function of VGAM473 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM473 include diagnosis, prevention and treatment of viral infection by Acyrthosiphon pisum virus. Specific functions, and accordingly utilities, of VGAM473 correlate with, and may be deduced from, the identity of the host target genes which VGAM473 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6586] Nucleotide sequences of the VGAM473 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM473 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM473 are further described hereinbelow with reference to Table 1.

[6587] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM473 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6588] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 474 (VGAM474) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6589] VGAM474 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM474 was detected is described hereinabove with reference to Figs. 2–8.

[6590] VGAM474 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Acyrthosiphon pisum virus. VGAM474 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6591] VGAM474 gene, herein designated VGAM GENE, encodes a VGAM474 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM474 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM474 precursor RNA is designated SEQ ID:13073, and is provided hereinbelow with reference to the sequence listing part.

[6592] VGAM474 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6593] An enzyme complex designated DICER COMPLEX, dices the VGAM474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM474 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM474 RNA is designated SEQ ID:13074, and is provided hereinbelow with reference to the sequence listing part.

[6594] VGAM474 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM474 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM474 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6595] VGAM474 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM474 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM474 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM474 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM474 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6596] The complementary binding of VGAM474 RNA, herein designated VGAM RNA, to host target binding sites on VGAM474 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM474 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM474 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6597] It is appreciated that VGAM474 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM474 host target genes. The mRNA of each one of this plurality of VGAM474 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM474 RNA, herein designated VGAM RNA, and which when bound by VGAM474 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM474 host target proteins.

[6598] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM474 gene, herein designated VGAM GENE, on one or more VGAM474 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[6599] It is yet further appreciated that a function of VGAM474 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM474 include diagnosis, prevention and treatment of viral infection by Acyrthosiphon pisum virus. Specific functions, and accordingly utilities, of VGAM474 correlate with, and may be deduced from, the identity of the host target genes which VGAM474 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6600] Nucleotide sequences of the VGAM474 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM474 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM474 are further described hereinbelow with reference to Table 1.

[6601] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM474 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6602] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 475 (VGAM475) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6603] VGAM475 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM475 was detected is described hereinabove with reference to Figs. 2–8.

[6604] VGAM475 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM475 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6605] VGAM475 gene, herein designated VGAM GENE, encodes a VGAM475 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM475 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM475 precursor RNA is designated SEQ ID:13083, and is provided hereinbelow with reference to the sequence listing part.

[6606] VGAM475 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM475 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6607] An enzyme complex designated DICER COMPLEX, dices the VGAM475 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM475 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM475 RNA is designated SEQ ID:13084, and is provided hereinbelow with reference to the sequence listing part.

[6608] VGAM475 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM475 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM475 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6609] VGAM475 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM475 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM475 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM475 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM475 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6610] The complementary binding of VGAM475 RNA, herein designated VGAM RNA, to host target binding sites on VGAM475 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM475 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM475 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6611] It is appreciated that VGAM475 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM475 host target genes. The mRNA of

each one of this plurality of VGAM475 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM475 RNA, herein designated VGAM RNA, and which when bound by VGAM475 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM475 host target proteins.

[6612] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM475 gene, herein designated VGAM GENE, on one or more VGAM475 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[6613] It is yet further appreciated that a function of VGAM475 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM475 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM475 correlate with, and may be deduced from, the identity of the host target genes which VGAM475 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6614] Nucleotide sequences of the VGAM475 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM475 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM475 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM475 are further described hereinbelow with reference to Table 1.

[6615] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM475 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[6616] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 476 (VGAM476) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6617] VGAM476 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM476 was detected is described hereinabove with reference to Figs. 2–8.

[6618] VGAM476 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM476 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6619] VGAM476 gene, herein designated VGAM GENE, encodes a VGAM476 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM476 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM476 precursor RNA is designated SEQ ID:13095, and is provided hereinbelow with reference to the sequence listing part.

[6620] VGAM476 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM476 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6621] An enzyme complex designated DICER COMPLEX, dices the VGAM476 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM476 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM476 RNA is designated SEQ ID:13096, and

is provided hereinbelow with reference to the sequence listing part.

[6622] VGAM476 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM476 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM476 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6623] VGAM476 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM476 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM476 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM476 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM476 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6624] The complementary binding of VGAM476 RNA, herein designated VGAM RNA, to host target binding sites on VGAM476 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM476 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM476 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6625] It is appreciated that VGAM476 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM476 host target genes. The mRNA of each one of this plurality of VGAM476 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM476 RNA, herein designated VGAM RNA, and which when bound by VGAM476 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM476 host target proteins.

[6626] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM476 gene, herein designated VGAM GENE, on one or more VGAM476 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6627] It is yet further appreciated that a function of VGAM476 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM476 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM476 correlate with, and may be deduced from, the identity of the host target genes which VGAM476 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6628] Nucleotide sequences of the VGAM476 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM476 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM476 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM476 are further described hereinbelow with reference to Table 1.

[6629] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM476 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6630] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 477 (VGAM477) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6631] VGAM477 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM477 was detected is described hereinabove with reference to Figs. 2–8.

[6632] VGAM477 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM477 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6633] VGAM477 gene, herein designated VGAM GENE, encodes a VGAM477 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM477 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM477 precursor RNA is

designated SEQ ID:13120, and is provided hereinbelow with reference to the sequence listing part.

[6634] VGAM477 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6635] An enzyme complex designated DICER COMPLEX, dices the VGAM477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM477 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM477 RNA is designated SEQ ID:13121, and is provided hereinbelow with reference to the sequence



listing part.

[6636] VGAM477 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM477 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM477 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6637] VGAM477 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM477 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM477 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM477 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM477 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6638] The complementary binding of VGAM477 RNA, herein designated VGAM RNA, to host target binding sites on VGAM477 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM477 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM477 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6639] It is appreciated that VGAM477 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM477 host target genes. The mRNA of each one of this plurality of VGAM477 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM477 RNA, herein designated VGAM RNA, and which when bound by VGAM477 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM477 host target proteins.

[6640] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM477 gene, herein designated VGAM GENE, on one or more VGAM477 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6641] It is yet further appreciated that a function of VGAM477 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM477 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM477 correlate with, and may be deduced from, the identity of the host target genes which VGAM477 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[6642] Nucleotide sequences of the VGAM477 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM477 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM477 are further described hereinbelow with reference to Table 1.

[6643] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM477 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6644] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 478 (VGAM478) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6645] VGAM478 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM478 was detected is described hereinabove with reference to Figs. 2–8.

[6646] VGAM478 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM478 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6647] VGAM478 gene, herein designated VGAM GENE, encodes a VGAM478 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM478 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM478 precursor RNA is designated SEQ ID:13123, and is provided hereinbelow

with reference to the sequence listing part.

[6648] VGAM478 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6649] An enzyme complex designated DICER COMPLEX, dices the VGAM478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM478 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM478 RNA is designated SEQ ID:13121, and is provided hereinbelow with reference to the sequence listing part.

[6650] VGAM478 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM478 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM478 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6651] VGAM478 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM478 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM478 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM478 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM478 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6652] The complementary binding of VGAM478 RNA, herein designated VGAM RNA, to host target binding sites on VGAM478 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM478 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM478 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6653] It is appreciated that VGAM478 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM478 host target genes. The mRNA of each one of this plurality of VGAM478 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM478 RNA, herein designated VGAM RNA, and which when bound by VGAM478 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM478 host target proteins.

[6654] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM478 gene, herein designated VGAM GENE, on one or more VGAM478 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6655] It is yet further appreciated that a function of VGAM478 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM478 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM478 correlate with, and may be deduced from, the identity of the host target genes which VGAM478 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6656] Nucleotide sequences of the VGAM478 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM478 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM478 are further described hereinbelow with reference to Table 1.

[6657] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM478 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6658] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 479 (VGAM479) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6659] VGAM479 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM479 was detected is described hereinabove with reference to Figs. 2–8.

[6660] VGAM479 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM479 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6661] VGAM479 gene, herein designated VGAM GENE, encodes a VGAM479 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM479 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM479 precursor RNA is designated SEQ ID:13124, and is provided hereinbelow with reference to the sequence listing part.

[6662] VGAM479 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM479 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6663] An enzyme complex designated DICER COMPLEX, dices the VGAM479 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM479 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM479 RNA is designated SEQ ID:13125, and is provided hereinbelow with reference to the sequence listing part.

[6664] VGAM479 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM479 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM479 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6665] VGAM479 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM479 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM479 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM479 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM479 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6666] The complementary binding of VGAM479 RNA, herein designated VGAM RNA, to host target binding sites on VGAM479 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM479 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM479 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6667] It is appreciated that VGAM479 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM479 host target genes. The mRNA of each one of this plurality of VGAM479 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM479 RNA, herein designated VGAM

RNA, and which when bound by VGAM479 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM479 host target proteins.

[6668] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM479 gene, herein designated VGAM GENE, on one or more VGAM479 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6669] It is yet further appreciated that a function of VGAM479 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM479 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM479 correlate with, and may be deduced from, the identity of the host target genes which VGAM479 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6670] Nucleotide sequences of the VGAM479 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM479 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM479 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM479 are further described hereinbelow with reference to Table 1.

[6671] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM479 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6672] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 480 (VGAM480) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6673] VGAM480 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM480 was detected is described hereinabove with reference to Figs. 2–8.

[6674] VGAM480 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM480 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6675] VGAM480 gene, herein designated VGAM GENE, encodes a VGAM480 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM480 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM480 precursor RNA is designated SEQ ID:13130, and is provided hereinbelow with reference to the sequence listing part.

[6676] VGAM480 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6677] An enzyme complex designated DICER COMPLEX, dices the VGAM480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM480 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM480 RNA is designated SEQ ID:13131, and is provided hereinbelow with reference to the sequence listing part.

[6678] VGAM480 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM480 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM480 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6679] VGAM480 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM480 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM480 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM480 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM480 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6680] The complementary binding of VGAM480 RNA, herein designated VGAM RNA, to host target binding sites on VGAM480 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM480 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM480 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6681] It is appreciated that VGAM480 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM480 host target genes. The mRNA of each one of this plurality of VGAM480 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM480 RNA, herein designated VGAM RNA, and which when bound by VGAM480 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM480 host target proteins.

[6682] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM480 gene, herein designated VGAM GENE, on one or more VGAM480 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6683] It is yet further appreciated that a function of VGAM480 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM480 include diagnosis, prevention and

treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM480 correlate with, and may be deduced from, the identity of the host target genes which VGAM480 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6684] Nucleotide sequences of the VGAM480 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM480 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM480 are further described hereinbelow with reference to Table 1.

[6685] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM480 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6686] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 481 (VGAM481) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6687] VGAM481 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM481 was detected is described hereinabove with reference to Figs. 2–8.

[6688] VGAM481 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM481 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6689] VGAM481 gene, herein designated VGAM GENE, encodes a VGAM481 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM481 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM481 precursor RNA is designated SEQ ID:13138, and is provided hereinbelow with reference to the sequence listing part.

[6690] VGAM481 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM481 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6691] An enzyme complex designated DICER COMPLEX, dices the VGAM481 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM481 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM481 RNA is designated SEQ ID:13139, and is provided hereinbelow with reference to the sequence listing part.

[6692] VGAM481 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM481 host target RNA, herein designated VGAM



HOST TARGET RNA. VGAM481 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6693] VGAM481 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM481 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM481 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM481 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM481 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6694] The complementary binding of VGAM481 RNA, herein designated VGAM RNA, to host target binding sites on VGAM481 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM481 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM481 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6695] It is appreciated that VGAM481 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM481 host target genes. The mRNA of each one of this plurality of VGAM481 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM481 RNA, herein designated VGAM RNA, and which when bound by VGAM481 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM481 host target proteins.

[6696] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM481 gene, herein designated VGAM GENE, on one or more VGAM481 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6697] It is yet further appreciated that a function of VGAM481 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM481 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific

functions, and accordingly utilities, of VGAM481 correlate with, and may be deduced from, the identity of the host target genes which VGAM481 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6698] Nucleotide sequences of the VGAM481 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM481 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM481 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM481 are further described hereinbelow with reference to Table 1.

[6699] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM481 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6700] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 482 (VGAM482) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[6701] VGAM482 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM482 was detected is described hereinabove with reference to Figs. 2–8.

[6702] VGAM482 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM482 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6703] VGAM482 gene, herein designated VGAM GENE, encodes a VGAM482 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM482 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM482 precursor RNA is designated SEQ ID:13146, and is provided hereinbelow with reference to the sequence listing part.

[6704] VGAM482 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM482 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6705] An enzyme complex designated DICER COMPLEX, dices the VGAM482 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM482 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM482 RNA is designated SEQ ID:13147, and is provided hereinbelow with reference to the sequence listing part.

[6706] VGAM482 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM482 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM482 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6707] VGAM482 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM482 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM482 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM482 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM482 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6708] The complementary binding of VGAM482 RNA, herein designated VGAM RNA, to host target binding sites on VGAM482 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM482 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM482 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6709] It is appreciated that VGAM482 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM482 host target genes. The mRNA of each one of this plurality of VGAM482 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM482 RNA, herein designated VGAM RNA, and which when bound by VGAM482 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM482 host target proteins.



[6710] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM482 gene, herein designated VGAM GENE, on one or more VGAM482 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6711] It is yet further appreciated that a function of VGAM482 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM482 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM482 correlate

with, and may be deduced from, the identity of the host target genes which VGAM482 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6712] Nucleotide sequences of the VGAM482 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM482 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM482 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM482 are further described hereinbelow with reference to Table 1.

[6713] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM482 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6714] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 483 (VGAM483) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[6715] VGAM483 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM483 was detected is described hereinabove with reference to Figs. 2–8.

[6716] VGAM483 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM483 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6717] VGAM483 gene, herein designated VGAM GENE, encodes a VGAM483 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM483 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM483 precursor RNA is designated SEQ ID:13152, and is provided hereinbelow with reference to the sequence listing part.

[6718] VGAM483 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6719] An enzyme complex designated DICER COMPLEX, dices the VGAM483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM483 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM483 RNA is designated SEQ ID:13147, and is provided hereinbelow with reference to the sequence listing part.

[6720] VGAM483 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM483 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM483 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6721] VGAM483 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM483 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM483 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM483 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM483 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6722] The complementary binding of VGAM483 RNA, herein designated VGAM RNA, to host target binding sites on VGAM483 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM483 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM483 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6723] It is appreciated that VGAM483 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM483 host target genes. The mRNA of each one of this plurality of VGAM483 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM483 RNA, herein designated VGAM RNA, and which when bound by VGAM483 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM483 host target proteins.

[6724] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM483 gene, herein designated VGAM GENE, on one or more VGAM483 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6725] It is yet further appreciated that a function of VGAM483 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM483 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM483 correlate with, and may be deduced from, the identity of the host

target genes which VGAM483 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6726] Nucleotide sequences of the VGAM483 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM483 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM483 are further described hereinbelow with reference to Table 1.

[6727] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM483 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6728] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 484 (VGAM484) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[6729] VGAM484 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM484 was detected is described hereinabove with reference to Figs. 2–8.

[6730] VGAM484 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM484 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6731] VGAM484 gene, herein designated VGAM GENE, encodes a VGAM484 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM484 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM484 precursor RNA is designated SEQ ID:13153, and is provided hereinbelow with reference to the sequence listing part.

[6732] VGAM484 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM484 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6733] An enzyme complex designated DICER COMPLEX, dices the VGAM484 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM484 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM484 RNA is designated SEQ ID:13154, and is provided hereinbelow with reference to the sequence listing part.

[6734] VGAM484 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM484 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM484 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6735] VGAM484 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM484 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM484 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM484 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM484 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6736] The complementary binding of VGAM484 RNA, herein designated VGAM RNA, to host target binding sites on VGAM484 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM484 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM484 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6737] It is appreciated that VGAM484 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM484 host target genes. The mRNA of each one of this plurality of VGAM484 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM484 RNA, herein designated VGAM RNA, and which when bound by VGAM484 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM484 host target proteins.

[6738] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM484 gene, herein designated VGAM GENE, on one or more VGAM484 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6739] It is yet further appreciated that a function of VGAM484 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM484 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM484 correlate with, and may be deduced from, the identity of the host target genes which VGAM484 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[6740] Nucleotide sequences of the VGAM484 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM484 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM484 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM484 are further described hereinbelow with reference to Table 1.

[6741] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM484 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6742] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 485 (VGAM485) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6743] VGAM485 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM485 was detected is described hereinabove with reference to Figs. 2–8.

[6744] VGAM485 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM485 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6745] VGAM485 gene, herein designated VGAM GENE, encodes a VGAM485 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM485 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM485 precursor RNA is designated SEQ ID:13168, and is provided hereinbelow with reference to the sequence listing part.

[6746] VGAM485 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM485 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6747] An enzyme complex designated DICER COMPLEX, dices the VGAM485 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM485 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM485 RNA is designated SEQ ID:13169, and is provided hereinbelow with reference to the sequence listing part.

[6748] VGAM485 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM485 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM485 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6749] VGAM485 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM485 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM485 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM485 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM485 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[6750] The complementary binding of VGAM485 RNA, herein designated VGAM RNA, to host target binding sites on VGAM485 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM485 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM485 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6751] It is appreciated that VGAM485 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM485 host target genes. The mRNA of each one of this plurality of VGAM485 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM485 RNA, herein designated VGAM RNA, and which when bound by VGAM485 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM485 host target proteins.

[6752] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM485 gene, herein designated VGAM GENE, on one or more VGAM485 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6753] It is yet further appreciated that a function of VGAM485 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM485 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM485 correlate with, and may be deduced from, the identity of the host target genes which VGAM485 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[6754] Nucleotide sequences of the VGAM485 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM485 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM485 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM485 are further described hereinbelow with reference to Table 1.

[6755] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM485 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6756] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 486 (VGAM486) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6757] VGAM486 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM486 was detected is described hereinabove with reference to Figs. 2–8.

[6758] VGAM486 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM486 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6759] VGAM486 gene, herein designated VGAM GENE, encodes a VGAM486 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM486 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM486 precursor RNA is designated SEQ ID:13178, and is provided hereinbelow with reference to the sequence listing part.

[6760] VGAM486 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM486 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6761] An enzyme complex designated DICER COMPLEX, dices the VGAM486 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM486 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM486 RNA is designated SEQ ID:13179, and is provided hereinbelow with reference to the sequence listing part.

[6762] VGAM486 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM486 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM486 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[6763] VGAM486 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM486 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM486 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM486 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM486 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6764] The complementary binding of VGAM486 RNA, herein designated VGAM RNA, to host target binding sites on VGAM486 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM486 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM486 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6765] It is appreciated that VGAM486 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM486 host target genes. The mRNA of each one of this plurality of VGAM486 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM486 RNA, herein designated VGAM RNA, and which when bound by VGAM486 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM486 host target proteins.

[6766] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM486 gene, herein designated VGAM GENE, on one or



more VGAM486 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6767] It is yet further appreciated that a function of VGAM486 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM486 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM486 correlate with, and may be deduced from, the identity of the host target genes which VGAM486 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6768] Nucleotide sequences of the VGAM486 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM486 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM486 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM486 are further described hereinbelow with reference to Table 1.

[6769] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM486 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6770] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 487 (VGAM487) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6771] VGAM487 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM487 was detected is described

hereinabove with reference to Figs. 2–8.

[6772] VGAM487 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM487 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6773] VGAM487 gene, herein designated VGAM GENE, encodes a VGAM487 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM487 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM487 precursor RNA is designated SEQ ID:13182, and is provided hereinbelow with reference to the sequence listing part.

[6774] VGAM487 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6775] An enzyme complex designated DICER COMPLEX, dices the VGAM487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM487 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM487 RNA is designated SEQ ID:13183, and is provided hereinbelow with reference to the sequence listing part.

[6776] VGAM487 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM487 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM487 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6777] VGAM487 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM487 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM487 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM487 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM487 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6778] The complementary binding of VGAM487 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM487 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM487 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM487 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6779] It is appreciated that VGAM487 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM487 host target genes. The mRNA of each one of this plurality of VGAM487 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM487 RNA, herein designated VGAM RNA, and which when bound by VGAM487 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM487 host target proteins.

[6780] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM487 gene, herein designated VGAM GENE, on one or more VGAM487 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6781] It is yet further appreciated that a function of VGAM487 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM487 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM487 correlate with, and may be deduced from, the identity of the host target genes which VGAM487 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6782] Nucleotide sequences of the VGAM487 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM487 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM487 are further described hereinbelow with reference to Table 1.

[6783] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM487 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6784] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 488 (VGAM488) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6785] VGAM488 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM488 was detected is described hereinabove with reference to Figs. 2-8.



[6786] VGAM488 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM488 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6787] VGAM488 gene, herein designated VGAM GENE, encodes a VGAM488 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM488 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM488 precursor RNA is designated SEQ ID:13220, and is provided hereinbelow with reference to the sequence listing part.

[6788] VGAM488 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[6789] An enzyme complex designated DICER COMPLEX, dices the VGAM488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM488 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM488 RNA is designated SEQ ID:13221, and is provided hereinbelow with reference to the sequence listing part.

[6790] VGAM488 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM488 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM488 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6791] VGAM488 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM488 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM488 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM488 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM488 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6792] The complementary binding of VGAM488 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM488 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM488 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM488 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6793] It is appreciated that VGAM488 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM488 host target genes. The mRNA of each one of this plurality of VGAM488 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM488 RNA, herein designated VGAM RNA, and which when bound by VGAM488 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM488 host target proteins.

[6794] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM488 gene, herein designated VGAM GENE, on one or more VGAM488 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6795] It is yet further appreciated that a function of VGAM488 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM488 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM488 correlate with, and may be deduced from, the identity of the host target genes which VGAM488 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6796] Nucleotide sequences of the VGAM488 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM488 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM488 are further described hereinbelow with reference to Table 1.

[6797] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM488 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6798] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 489 (VGAM489) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6799] VGAM489 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM489 was detected is described hereinabove with reference to Figs. 2-8.

[6800] VGAM489 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of African swine fever virus. VGAM489 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6801] VGAM489 gene, herein designated VGAM GENE, encodes a VGAM489 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM489 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM489 precursor RNA is designated SEQ ID:13233, and is provided hereinbelow with reference to the sequence listing part.

[6802] VGAM489 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6803] An enzyme complex designated DICER COMPLEX, dices the VGAM489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM489 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM489 RNA is designated SEQ ID:13221, and is provided hereinbelow with reference to the sequence listing part.

[6804] VGAM489 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM489 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM489 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6805] VGAM489 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM489 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM489 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM489 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM489 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6806] The complementary binding of VGAM489 RNA, herein designated VGAM RNA, to host target binding sites on VGAM489 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM489 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM489 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6807] It is appreciated that VGAM489 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM489 host target genes. The mRNA of each one of this plurality of VGAM489 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM489 RNA, herein designated VGAM RNA, and which when bound by VGAM489 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM489 host target proteins.

[6808] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM489 gene, herein designated VGAM GENE, on one or more VGAM489 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6809] It is yet further appreciated that a function of VGAM489 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM489 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM489 correlate with, and may be deduced from, the identity of the host target genes which VGAM489 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6810] Nucleotide sequences of the VGAM489 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM489 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM489 are further described hereinbelow with reference to Table 1.

[6811] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM489 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6812] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 490 (VGAM490) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6813] VGAM490 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM490 was detected is described hereinabove with reference to Figs. 2-8.

[6814] VGAM490 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever

virus. VGAM490 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6815] VGAM490 gene, herein designated VGAM GENE, encodes a VGAM490 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM490 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM490 precursor RNA is designated SEQ ID:13234, and is provided hereinbelow with reference to the sequence listing part.

[6816] VGAM490 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6817] An enzyme complex designated DICER COMPLEX, dices

the VGAM490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM490 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM490 RNA is designated SEQ ID:13235, and is provided hereinbelow with reference to the sequence listing part.

[6818] VGAM490 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM490 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM490 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6819] VGAM490 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM490 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM490 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM490 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM490 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6820] The complementary binding of VGAM490 RNA, herein designated VGAM RNA, to host target binding sites on VGAM490 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM490 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM490 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6821] It is appreciated that VGAM490 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM490 host target genes. The mRNA of each one of this plurality of VGAM490 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM490 RNA, herein designated VGAM RNA, and which when bound by VGAM490 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM490 host target proteins.

[6822] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM490 gene, herein designated VGAM GENE, on one or more VGAM490 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6823] It is yet further appreciated that a function of VGAM490 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM490 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM490 correlate with, and may be deduced from, the identity of the host target genes which VGAM490 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6824] Nucleotide sequences of the VGAM490 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM490 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM490 are further described hereinbelow with reference to Table 1.

[6825] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM490 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6826] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 491 (VGAM491) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6827] VGAM491 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM491 was detected is described hereinabove with reference to Figs. 2-8.

[6828] VGAM491 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P virus. VGAM491 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[6829] VGAM491 gene, herein designated VGAM GENE, encodes a VGAM491 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM491 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM491 precursor RNA is designated SEQ ID:13257, and is provided hereinbelow with reference to the sequence listing part.

[6830] VGAM491 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM491 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6831] An enzyme complex designated DICER COMPLEX, dices the VGAM491 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM491 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM491 RNA is designated SEQ ID:13258, and is provided hereinbelow with reference to the sequence listing part.

[6832] VGAM491 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM491 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM491 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6833] VGAM491 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM491 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM491 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM491 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM491 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6834] The complementary binding of VGAM491 RNA, herein designated VGAM RNA, to host target binding sites on VGAM491 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM491 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM491 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6835] It is appreciated that VGAM491 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM491 host target genes. The mRNA of each one of this plurality of VGAM491 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM491 RNA, herein designated VGAM RNA, and which when bound by VGAM491 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM491 host target proteins.

[6836] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM491 gene, herein designated VGAM GENE, on one or more VGAM491 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6837] It is yet further appreciated that a function of VGAM491 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM491 include diagnosis, prevention and treatment of viral infection by Himetobi P virus. Specific functions, and accordingly utilities, of VGAM491 correlate with, and may be deduced from, the identity of the host target genes which VGAM491 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6838] Nucleotide sequences of the VGAM491 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM491 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM491 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM491 are further described hereinbelow with reference to Table 1.

[6839] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM491 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6840] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 492 (VGAM492) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6841] VGAM492 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM492 was detected is described hereinabove with reference to Figs. 2-8.

[6842] VGAM492 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM492 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[6843] VGAM492 gene, herein designated VGAM GENE, encodes a VGAM492 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM492 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM492 precursor RNA is designated SEQ ID:13261, and is provided hereinbelow with reference to the sequence listing part.

[6844] VGAM492 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6845] An enzyme complex designated DICER COMPLEX, dices the VGAM492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM492 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM492 RNA is designated SEQ ID:13262, and is provided hereinbelow with reference to the sequence listing part.

[6846] VGAM492 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM492 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM492 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6847] VGAM492 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM492 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM492 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM492 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM492 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6848] The complementary binding of VGAM492 RNA, herein designated VGAM RNA, to host target binding sites on VGAM492 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM492 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM492 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6849] It is appreciated that VGAM492 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM492 host target genes. The mRNA of each one of this plurality of VGAM492 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM492 RNA, herein designated VGAM RNA, and which when bound by VGAM492 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM492 host target proteins.

[6850] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM492 gene, herein designated VGAM GENE, on one or more VGAM492 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6851] It is yet further appreciated that a function of VGAM492 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM492 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM492 correlate with, and may be deduced from, the identity of the host target genes which VGAM492 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6852] Nucleotide sequences of the VGAM492 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM492 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM492 are further de-

scribed hereinbelow with reference to Table 1.

[6853] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM492 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6854] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 493 (VGAM493) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6855] VGAM493 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM493 was detected is described hereinabove with reference to Figs. 2-8.

[6856] VGAM493 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus. VGAM493 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6857] VGAM493 gene, herein designated VGAM GENE, encodes a VGAM493 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM493 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM493 precursor RNA is designated SEQ ID:13268, and is provided hereinbelow with reference to the sequence listing part.

[6858] VGAM493 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM493 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6859] An enzyme complex designated DICER COMPLEX, dices the VGAM493 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM493 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM493 RNA is designated SEQ ID:13269, and is provided hereinbelow with reference to the sequence listing part.

[6860] VGAM493 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM493 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM493 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6861] VGAM493 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM493 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM493 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM493 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM493 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6862] The complementary binding of VGAM493 RNA, herein designated VGAM RNA, to host target binding sites on VGAM493 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM493 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM493 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6863] It is appreciated that VGAM493 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM493 host target genes. The mRNA of each one of this plurality of VGAM493 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM493 RNA, herein designated VGAM RNA, and which when bound by VGAM493 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM493 host target proteins.

[6864] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM493 gene, herein designated VGAM GENE, on one or more VGAM493 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6865] It is yet further appreciated that a function of VGAM493 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM493 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM493 correlate with, and may be deduced from, the identity of the host target genes which VGAM493 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6866] Nucleotide sequences of the VGAM493 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM493 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM493 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM493 are further described hereinbelow with reference to Table 1.

[6867] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM493 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6868] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 494 (VGAM494) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6869] VGAM494 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM494 was detected is described hereinabove with reference to Figs. 2-8.

[6870] VGAM494 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P virus. VGAM494 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6871] VGAM494 gene, herein designated VGAM GENE, encodes a

VGAM494 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM494 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM494 precursor RNA is designated SEQ ID:13279, and is provided hereinbelow with reference to the sequence listing part.

[6872] VGAM494 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6873] An enzyme complex designated DICER COMPLEX, dices the VGAM494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM494 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM494 RNA is designated SEQ ID:13280, and is provided hereinbelow with reference to the sequence listing part.

[6874] VGAM494 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM494 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM494 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6875] VGAM494 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM494 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM494 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM494 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM494 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6876] The complementary binding of VGAM494 RNA, herein designated VGAM RNA, to host target binding sites on VGAM494 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM494 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM494 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[6877] It is appreciated that VGAM494 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM494 host target genes. The mRNA of each one of this plurality of VGAM494 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM494 RNA, herein designated VGAM RNA, and which when bound by VGAM494 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM494 host target proteins.

[6878] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM494 gene, herein designated VGAM GENE, on one or more VGAM494 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6879] It is yet further appreciated that a function of VGAM494 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM494 include diagnosis, prevention and treatment of viral infection by Himetobi P virus. Specific functions, and accordingly utilities, of VGAM494 correlate with, and may be deduced from, the identity of the host target genes which VGAM494 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6880] Nucleotide sequences of the VGAM494 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM494 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM494 are further described hereinbelow with reference to Table 1.

[6881] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM494 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6882] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 495 (VGAM495) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6883] VGAM495 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM495 was detected is described hereinabove with reference to Figs. 2-8.

[6884] VGAM495 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P virus. VGAM495 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6885] VGAM495 gene, herein designated VGAM GENE, encodes a VGAM495 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM495 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM495 precursor RNA is designated SEQ ID:13293, and is provided hereinbelow with reference to the sequence listing part.

[6886] VGAM495 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6887] An enzyme complex designated DICER COMPLEX, dices the VGAM495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM495 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM495 RNA is designated SEQ ID:13294, and is provided hereinbelow with reference to the sequence listing part.

[6888] VGAM495 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM495 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM495 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6889] VGAM495 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM495 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM495 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM495 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM495 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6890] The complementary binding of VGAM495 RNA, herein designated VGAM RNA, to host target binding sites on VGAM495 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM495 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM495 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6891] It is appreciated that VGAM495 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM495 host target genes. The mRNA of each one of this plurality of VGAM495 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM495 RNA, herein designated VGAM RNA, and which when bound by VGAM495 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM495 host target proteins.

[6892] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM495 gene, herein designated VGAM GENE, on one or more VGAM495 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6893] It is yet further appreciated that a function of VGAM495 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM495 include diagnosis, prevention and treatment of viral infection by Himetobi P virus. Specific functions, and accordingly utilities, of VGAM495 correlate with, and may be deduced from, the identity of the host target genes which VGAM495 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6894] Nucleotide sequences of the VGAM495 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM495 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM495 are further described hereinbelow with reference to Table 1.

[6895] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM495 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6896] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 496 (VGAM496) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6897] VGAM496 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM496 was detected is described hereinabove with reference to Figs. 2–8.

[6898] VGAM496 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM496 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6899] VGAM496 gene, herein designated VGAM GENE, encodes a VGAM496 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike



most ordinary genes, VGAM496 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM496 precursor RNA is designated SEQ ID:13297, and is provided hereinbelow with reference to the sequence listing part.

[6900] VGAM496 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6901] An enzyme complex designated DICER COMPLEX, dices the VGAM496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM496 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM496 RNA is designated SEQ ID:13298, and is provided hereinbelow with reference to the sequence listing part.

[6902] VGAM496 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM496 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM496 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6903] VGAM496 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM496 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM496 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM496 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM496 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6904] The complementary binding of VGAM496 RNA, herein designated VGAM RNA, to host target binding sites on VGAM496 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM496 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM496 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6905] It is appreciated that VGAM496 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM496 host target genes. The mRNA of each one of this plurality of VGAM496 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM496 RNA, herein designated VGAM RNA, and which when bound by VGAM496 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM496 host target proteins.

[6906] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM496 gene, herein designated VGAM GENE, on one or more VGAM496 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6907] It is yet further appreciated that a function of VGAM496 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM496 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM496 correlate with, and may be deduced from, the identity of the host target genes which VGAM496 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6908] Nucleotide sequences of the VGAM496 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM496 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM496 are further described hereinbelow with reference to Table 1.

[6909] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM496 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6910] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 497 (VGAM497) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6911] VGAM497 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM497 was detected is described hereinabove with reference to Figs. 2–8.

[6912] VGAM497 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human foamy virus. VGAM497 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6913] VGAM497 gene, herein designated VGAM GENE, encodes a VGAM497 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM497 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM497 precursor RNA is designated SEQ ID:13327, and is provided hereinbelow with reference to the sequence listing part.

[6914] VGAM497 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6915] An enzyme complex designated DICER COMPLEX, dices the VGAM497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM497 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM497 RNA is designated SEQ ID:13328, and is provided hereinbelow with reference to the sequence listing part.

[6916] VGAM497 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM497 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM497 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6917] VGAM497 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM497 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM497 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM497 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM497 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6918] The complementary binding of VGAM497 RNA, herein designated VGAM RNA, to host target binding sites on VGAM497 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM497 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM497 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6919] It is appreciated that VGAM497 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM497 host target genes. The mRNA of each one of this plurality of VGAM497 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM497 RNA, herein designated VGAM RNA, and which when bound by VGAM497 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM497 host target proteins.

[6920] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM497 gene, herein designated VGAM GENE, on one or more VGAM497 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [6921] It is yet further appreciated that a function of VGAM497 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM497 include diagnosis, prevention and treatment of viral infection by Human foamy virus. Specific functions, and accordingly utilities, of VGAM497 correlate with, and may be deduced from, the identity of the host target genes which VGAM497 binds and inhibits, and the function of these host target genes, as elaborated herein–below.
- [6922] Nucleotide sequences of the VGAM497 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM497 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM497 are further described hereinbelow with reference to Table 1.
- [6923] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM497 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6924] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 498 (VGAM498) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6925] VGAM498 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM498 was detected is described hereinabove with reference to Figs. 2–8.

[6926] VGAM498 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM498 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6927] VGAM498 gene, herein designated VGAM GENE, encodes a VGAM498 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM498 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM498 precursor RNA is designated SEQ ID:13373, and is provided hereinbelow with reference to the sequence listing part.

[6928] VGAM498 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM498 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6929] An enzyme complex designated DICER COMPLEX, dices the VGAM498 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM498 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM498 RNA is designated SEQ ID:13374, and is provided hereinbelow with reference to the sequence listing part.

[6930] VGAM498 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM498 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM498 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6931] VGAM498 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM498 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM498 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM498 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM498 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6932] The complementary binding of VGAM498 RNA, herein designated VGAM RNA, to host target binding sites on VGAM498 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM498 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM498 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6933] It is appreciated that VGAM498 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM498 host target genes. The mRNA of

each one of this plurality of VGAM498 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM498 RNA, herein designated VGAM RNA, and which when bound by VGAM498 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM498 host target proteins.

[6934] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM498 gene, herein designated VGAM GENE, on one or more VGAM498 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[6935] It is yet further appreciated that a function of VGAM498 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM498 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM498 correlate with, and may be deduced from, the identity of the host target genes which VGAM498 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6936] Nucleotide sequences of the VGAM498 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM498 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM498 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM498 are further described hereinbelow with reference to Table 1.

[6937] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM498 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[6938] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 499 (VGAM499) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6939] VGAM499 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM499 was detected is described hereinabove with reference to Figs. 2–8.

[6940] VGAM499 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM499 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6941] VGAM499 gene, herein designated VGAM GENE, encodes a VGAM499 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM499 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM499 precursor RNA is designated SEQ ID:13376, and is provided hereinbelow with reference to the sequence listing part.

[6942] VGAM499 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM499 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6943] An enzyme complex designated DICER COMPLEX, dices the VGAM499 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM499 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM499 RNA is designated SEQ ID:13377, and

is provided hereinbelow with reference to the sequence listing part.

[6944] VGAM499 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM499 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM499 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6945] VGAM499 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM499 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM499 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM499 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM499 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6946] The complementary binding of VGAM499 RNA, herein designated VGAM RNA, to host target binding sites on VGAM499 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM499 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM499 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6947] It is appreciated that VGAM499 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM499 host target genes. The mRNA of each one of this plurality of VGAM499 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM499 RNA, herein designated VGAM RNA, and which when bound by VGAM499 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM499 host target proteins.

[6948] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM499 gene, herein designated VGAM GENE, on one or more VGAM499 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6949] It is yet further appreciated that a function of VGAM499 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM499 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM499 correlate with, and may be deduced from, the identity of the host target genes which VGAM499 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6950] Nucleotide sequences of the VGAM499 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM499 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM499 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM499 are further described hereinbelow with reference to Table 1.

[6951] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM499 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6952] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 500 (VGAM500) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6953] VGAM500 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM500 was detected is described hereinabove with reference to Figs. 2–8.

[6954] VGAM500 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM500 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6955] VGAM500 gene, herein designated VGAM GENE, encodes a VGAM500 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM500 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM500 precursor RNA is



designated SEQ ID:13406, and is provided hereinbelow with reference to the sequence listing part.

[6956] VGAM500 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM500 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6957] An enzyme complex designated DICER COMPLEX, dices the VGAM500 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM500 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM500 RNA is designated SEQ ID:13407, and is provided hereinbelow with reference to the sequence

listing part.

[6958] VGAM500 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM500 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM500 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6959] VGAM500 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM500 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM500 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM500 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM500 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6960] The complementary binding of VGAM500 RNA, herein designated VGAM RNA, to host target binding sites on VGAM500 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM500 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM500 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6961] It is appreciated that VGAM500 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM500 host target genes. The mRNA of each one of this plurality of VGAM500 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM500 RNA, herein designated VGAM RNA, and which when bound by VGAM500 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM500 host target proteins.

[6962] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM500 gene, herein designated VGAM GENE, on one or more VGAM500 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6963] It is yet further appreciated that a function of VGAM500 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM500 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM500 correlate with, and may be deduced from, the identity of the host target genes which VGAM500 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6964] Nucleotide sequences of the VGAM500 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM500 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM500 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM500 are further described hereinbelow with reference to Table 1.

[6965] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM500 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6966] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 501 (VGAM501) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6967] VGAM501 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM501 was detected is described hereinabove with reference to Figs. 2–8.

[6968] VGAM501 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM501 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6969] VGAM501 gene, herein designated VGAM GENE, encodes a VGAM501 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM501 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM501 precursor RNA is designated SEQ ID:13414, and is provided hereinbelow

with reference to the sequence listing part.

[6970] VGAM501 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6971] An enzyme complex designated DICER COMPLEX, dices the VGAM501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM501 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM501 RNA is designated SEQ ID:13415, and is provided hereinbelow with reference to the sequence listing part.

[6972] VGAM501 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM501 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM501 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6973] VGAM501 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM501 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM501 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM501 RNA, herein designated



VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM501 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6974] The complementary binding of VGAM501 RNA, herein designated VGAM RNA, to host target binding sites on VGAM501 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM501 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM501 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6975] It is appreciated that VGAM501 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM501 host target genes. The mRNA of each one of this plurality of VGAM501 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM501 RNA, herein designated VGAM RNA, and which when bound by VGAM501 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM501 host target proteins.

[6976] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM501 gene, herein designated VGAM GENE, on one or more VGAM501 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6977] It is yet further appreciated that a function of VGAM501 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM501 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM501 correlate with, and may be deduced from, the identity of the host target genes which VGAM501 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6978] Nucleotide sequences of the VGAM501 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM501 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM501 are further described hereinbelow with reference to Table 1.

[6979] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM501 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6980] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 502 (VGAM502) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6981] VGAM502 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM502 was detected is described hereinabove with reference to Figs. 2–8.

[6982] VGAM502 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM502 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6983] VGAM502 gene, herein designated VGAM GENE, encodes a VGAM502 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM502 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM502 precursor RNA is designated SEQ ID:13420, and is provided hereinbelow with reference to the sequence listing part.

[6984] VGAM502 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM502 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6985] An enzyme complex designated DICER COMPLEX, dices the VGAM502 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM502 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM502 RNA is designated SEQ ID:13421, and is provided hereinbelow with reference to the sequence listing part.

[6986] VGAM502 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM502 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM502 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[6987] VGAM502 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM502 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM502 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM502 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM502 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[6988] The complementary binding of VGAM502 RNA, herein designated VGAM RNA, to host target binding sites on VGAM502 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM502 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM502 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6989] It is appreciated that VGAM502 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM502 host target genes. The mRNA of each one of this plurality of VGAM502 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM502 RNA, herein designated VGAM

RNA, and which when bound by VGAM502 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM502 host target proteins.

[6990] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM502 gene, herein designated VGAM GENE, on one or more VGAM502 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[6991] It is yet further appreciated that a function of VGAM502 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM502 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM502 correlate with, and may be deduced from, the identity of the host target genes which VGAM502 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6992] Nucleotide sequences of the VGAM502 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM502 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM502 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM502 are further described hereinbelow with reference to Table 1.

[6993] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM502 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6994] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 503 (VGAM503) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6995] VGAM503 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM503 was detected is described hereinabove with reference to Figs. 2–8.

[6996] VGAM503 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM503 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6997] VGAM503 gene, herein designated VGAM GENE, encodes a VGAM503 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM503 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM503 precursor RNA is designated SEQ ID:13430, and is provided hereinbelow with reference to the sequence listing part.

[6998] VGAM503 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6999] An enzyme complex designated DICER COMPLEX, dices the VGAM503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM503 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM503 RNA is designated SEQ ID:13431, and is provided hereinbelow with reference to the sequence listing part.

[7000] VGAM503 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM503 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM503 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7001] VGAM503 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM503 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM503 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM503 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM503 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7002] The complementary binding of VGAM503 RNA, herein designated VGAM RNA, to host target binding sites on VGAM503 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM503 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM503 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7003] It is appreciated that VGAM503 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM503 host target genes. The mRNA of each one of this plurality of VGAM503 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM503 RNA, herein designated VGAM RNA, and which when bound by VGAM503 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM503 host target proteins.

[7004] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM503 gene, herein designated VGAM GENE, on one or more VGAM503 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7005] It is yet further appreciated that a function of VGAM503 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM503 include diagnosis, prevention and

treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM503 correlate with, and may be deduced from, the identity of the host target genes which VGAM503 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7006] Nucleotide sequences of the VGAM503 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM503 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM503 are further described hereinbelow with reference to Table 1.

[7007] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM503 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7008] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 504 (VGAM504) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7009] VGAM504 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM504 was detected is described hereinabove with reference to Figs. 2–8.

[7010] VGAM504 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus. VGAM504 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7011] VGAM504 gene, herein designated VGAM GENE, encodes a VGAM504 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM504 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM504 precursor RNA is designated SEQ ID:13439, and is provided hereinbelow with reference to the sequence listing part.

[7012] VGAM504 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM504 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7013] An enzyme complex designated DICER COMPLEX, dices the VGAM504 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM504 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM504 RNA is designated SEQ ID:13440, and is provided hereinbelow with reference to the sequence listing part.

[7014] VGAM504 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM504 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM504 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7015] VGAM504 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM504 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM504 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM504 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM504 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7016] The complementary binding of VGAM504 RNA, herein designated VGAM RNA, to host target binding sites on VGAM504 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM504 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM504 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7017] It is appreciated that VGAM504 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM504 host target genes. The mRNA of each one of this plurality of VGAM504 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM504 RNA, herein designated VGAM RNA, and which when bound by VGAM504 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM504 host target proteins.

[7018] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM504 gene, herein designated VGAM GENE, on one or more VGAM504 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7019] It is yet further appreciated that a function of VGAM504 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM504 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific

functions, and accordingly utilities, of VGAM504 correlate with, and may be deduced from, the identity of the host target genes which VGAM504 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7020] Nucleotide sequences of the VGAM504 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM504 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM504 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM504 are further described hereinbelow with reference to Table 1.

[7021] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM504 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7022] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 505 (VGAM505) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[7023] VGAM505 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM505 was detected is described hereinabove with reference to Figs. 2–8.

[7024] VGAM505 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot mottle virus. VGAM505 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7025] VGAM505 gene, herein designated VGAM GENE, encodes a VGAM505 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM505 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM505 precursor RNA is designated SEQ ID:13547, and is provided hereinbelow with reference to the sequence listing part.

[7026] VGAM505 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM505 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7027] An enzyme complex designated DICER COMPLEX, dices the VGAM505 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM505 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM505 RNA is designated SEQ ID:13548, and is provided hereinbelow with reference to the sequence listing part.

[7028] VGAM505 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM505 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM505 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7029] VGAM505 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM505 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM505 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM505 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM505 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7030] The complementary binding of VGAM505 RNA, herein designated VGAM RNA, to host target binding sites on VGAM505 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM505 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM505 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7031] It is appreciated that VGAM505 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM505 host target genes. The mRNA of each one of this plurality of VGAM505 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM505 RNA, herein designated VGAM RNA, and which when bound by VGAM505 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM505 host target proteins.

[7032] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM505 gene, herein designated VGAM GENE, on one or more VGAM505 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7033] It is yet further appreciated that a function of VGAM505 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM505 include diagnosis, prevention and treatment of viral infection by Cocksfoot mottle virus. Specific functions, and accordingly utilities, of VGAM505

correlate with, and may be deduced from, the identity of the host target genes which VGAM505 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7034] Nucleotide sequences of the VGAM505 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM505 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM505 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM505 are further described hereinbelow with reference to Table 1.

[7035] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM505 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7036] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 506 (VGAM506) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[7037] VGAM506 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM506 was detected is described hereinabove with reference to Figs. 2–8.

[7038] VGAM506 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot mottle virus. VGAM506 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7039] VGAM506 gene, herein designated VGAM GENE, encodes a VGAM506 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM506 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM506 precursor RNA is designated SEQ ID:13583, and is provided hereinbelow with reference to the sequence listing part.

[7040] VGAM506 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7041] An enzyme complex designated DICER COMPLEX, dices the VGAM506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM506 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM506 RNA is designated SEQ ID:13584, and is provided hereinbelow with reference to the sequence listing part.

[7042] VGAM506 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM506 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM506 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7043] VGAM506 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM506 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM506 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM506 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM506 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7044] The complementary binding of VGAM506 RNA, herein designated VGAM RNA, to host target binding sites on VGAM506 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM506 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM506 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7045] It is appreciated that VGAM506 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM506 host target genes. The mRNA of each one of this plurality of VGAM506 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM506 RNA, herein designated VGAM RNA, and which when bound by VGAM506 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM506 host target proteins.

[7046] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM506 gene, herein designated VGAM GENE, on one or more VGAM506 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7047] It is yet further appreciated that a function of VGAM506 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM506 include diagnosis, prevention and treatment of viral infection by Cocksfoot mottle virus. Specific functions, and accordingly utilities, of VGAM506 correlate with, and may be deduced from, the identity of



the host target genes which VGAM506 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7048] Nucleotide sequences of the VGAM506 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM506 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM506 are further described hereinbelow with reference to Table 1.

[7049] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM506 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7050] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 507 (VGAM507) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7051] VGAM507 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM507 was detected is described hereinabove with reference to Figs. 2–8.

[7052] VGAM507 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot mottle virus. VGAM507 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7053] VGAM507 gene, herein designated VGAM GENE, encodes a VGAM507 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM507 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM507 precursor RNA is designated SEQ ID:13592, and is provided hereinbelow with reference to the sequence listing part.

[7054] VGAM507 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM507 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7055] An enzyme complex designated DICER COMPLEX, dices the VGAM507 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM507 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM507 RNA is designated SEQ ID:13593, and is provided hereinbelow with reference to the sequence listing part.

[7056] VGAM507 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM507 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM507 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7057] VGAM507 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM507 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM507 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM507 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM507 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7058] The complementary binding of VGAM507 RNA, herein designated VGAM RNA, to host target binding sites on VGAM507 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM507 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM507 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7059] It is appreciated that VGAM507 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM507 host target genes. The mRNA of each one of this plurality of VGAM507 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM507 RNA, herein designated VGAM RNA, and which when bound by VGAM507 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM507 host target proteins.

[7060] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM507 gene, herein designated VGAM GENE, on one or more VGAM507 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7061] It is yet further appreciated that a function of VGAM507 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM507 include diagnosis, prevention and treatment of viral infection by Cocksfoot mottle virus. Specific functions, and accordingly utilities, of VGAM507 correlate with, and may be deduced from, the identity of the host target genes which VGAM507 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[7062] Nucleotide sequences of the VGAM507 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM507 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM507 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM507 are further described hereinbelow with reference to Table 1.

[7063] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM507 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7064] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 508 (VGAM508) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7065] VGAM508 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM508 was detected is described hereinabove with reference to Figs. 2–8.

[7066] VGAM508 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot mottle virus. VGAM508 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7067] VGAM508 gene, herein designated VGAM GENE, encodes a VGAM508 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM508 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM508 precursor RNA is designated SEQ ID:13598, and is provided hereinbelow with reference to the sequence listing part.

[7068] VGAM508 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM508 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the



fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7069] An enzyme complex designated DICER COMPLEX, dices the VGAM508 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM508 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM508 RNA is designated SEQ ID:13599, and is provided hereinbelow with reference to the sequence listing part.

[7070] VGAM508 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM508 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM508 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7071] VGAM508 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM508 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM508 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM508 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM508 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[7072] The complementary binding of VGAM508 RNA, herein designated VGAM RNA, to host target binding sites on VGAM508 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM508 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM508 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7073] It is appreciated that VGAM508 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM508 host target genes. The mRNA of each one of this plurality of VGAM508 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM508 RNA, herein designated VGAM RNA, and which when bound by VGAM508 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM508 host target proteins.

[7074] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM508 gene, herein designated VGAM GENE, on one or more VGAM508 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7075] It is yet further appreciated that a function of VGAM508 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM508 include diagnosis, prevention and treatment of viral infection by Cocksfoot mottle virus. Specific functions, and accordingly utilities, of VGAM508 correlate with, and may be deduced from, the identity of the host target genes which VGAM508 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[7076] Nucleotide sequences of the VGAM508 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM508 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM508 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM508 are further described hereinbelow with reference to Table 1.

[7077] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM508 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7078] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 509 (VGAM509) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7079] VGAM509 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM509 was detected is described hereinabove with reference to Figs. 2–8.

[7080] VGAM509 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus.

VGAM509 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7081] VGAM509 gene, herein designated VGAM GENE, encodes a VGAM509 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM509 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM509 precursor RNA is designated SEQ ID:13611, and is provided hereinbelow with reference to the sequence listing part.

[7082] VGAM509 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7083] An enzyme complex designated DICER COMPLEX, dices the VGAM509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM509 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM509 RNA is designated SEQ ID:13612, and is provided hereinbelow with reference to the sequence listing part.

[7084] VGAM509 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM509 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM509 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[7085] VGAM509 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM509 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM509 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM509 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM509 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[7086] The complementary binding of VGAM509 RNA, herein designated VGAM RNA, to host target binding sites on VGAM509 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM509 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM509 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7087] It is appreciated that VGAM509 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM509 host target genes. The mRNA of each one of this plurality of VGAM509 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM509 RNA, herein designated VGAM RNA, and which when bound by VGAM509 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM509 host target proteins.

[7088] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM509 gene, herein designated VGAM GENE, on one or

more VGAM509 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7089] It is yet further appreciated that a function of VGAM509 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM509 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM509 correlate with, and may be deduced from, the identity of the host target genes which VGAM509 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7090] Nucleotide sequences of the VGAM509 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM509 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM509 are further described hereinbelow with reference to Table 1.

[7091] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM509 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7092] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 510 (VGAM510) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7093] VGAM510 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM510 was detected is described

hereinabove with reference to Figs. 2–8.

[7094] VGAM510 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM510 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7095] VGAM510 gene, herein designated VGAM GENE, encodes a VGAM510 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM510 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM510 precursor RNA is designated SEQ ID:13624, and is provided hereinbelow with reference to the sequence listing part.

[7096] VGAM510 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7097] An enzyme complex designated DICER COMPLEX, dices the VGAM510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM510 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM510 RNA is designated SEQ ID:13625, and is provided hereinbelow with reference to the sequence listing part.

[7098] VGAM510 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM510 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM510 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7099] VGAM510 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM510 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM510 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM510 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM510 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7100] The complementary binding of VGAM510 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM510 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM510 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM510 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7101] It is appreciated that VGAM510 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM510 host target genes. The mRNA of each one of this plurality of VGAM510 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM510 RNA, herein designated VGAM RNA, and which when bound by VGAM510 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM510 host target proteins.

[7102] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM510 gene, herein designated VGAM GENE, on one or more VGAM510 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7103] It is yet further appreciated that a function of VGAM510 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM510 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM510 correlate with, and may be deduced from, the identity of the host target genes which VGAM510 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7104] Nucleotide sequences of the VGAM510 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM510 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM510 are further described hereinbelow with reference to Table 1.

[7105] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM510 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7106] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 511 (VGAM511) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7107] VGAM511 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM511 was detected is described hereinabove with reference to Figs. 2-8.

[7108] VGAM511 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM511 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7109] VGAM511 gene, herein designated VGAM GENE, encodes a VGAM511 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM511 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM511 precursor RNA is designated SEQ ID:13657, and is provided hereinbelow with reference to the sequence listing part.

[7110] VGAM511 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[7111] An enzyme complex designated DICER COMPLEX, dices the VGAM511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM511 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM511 RNA is designated SEQ ID:13658, and is provided hereinbelow with reference to the sequence listing part.

[7112] VGAM511 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM511 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM511 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7113] VGAM511 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM511 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM511 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM511 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM511 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7114] The complementary binding of VGAM511 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM511 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM511 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM511 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7115] It is appreciated that VGAM511 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM511 host target genes. The mRNA of each one of this plurality of VGAM511 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM511 RNA, herein designated VGAM RNA, and which when bound by VGAM511 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM511 host target proteins.

[7116] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM511 gene, herein designated VGAM GENE, on one or more VGAM511 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7117] It is yet further appreciated that a function of VGAM511 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM511 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM511 correlate with, and may be deduced from, the identity of the host target genes which VGAM511 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7118] Nucleotide sequences of the VGAM511 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM511 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM511 are further described hereinbelow with reference to Table 1.

[7119] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM511 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7120] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 512 (VGAM512) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7121] VGAM512 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM512 was detected is described hereinabove with reference to Figs. 2-8.

[7122] VGAM512 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 1. VGAM512 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7123] VGAM512 gene, herein designated VGAM GENE, encodes a VGAM512 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM512 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM512 precursor RNA is designated SEQ ID:13700, and is provided hereinbelow with reference to the sequence listing part.

[7124] VGAM512 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[7125] An enzyme complex designated DICER COMPLEX, dices the VGAM512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM512 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM512 RNA is designated SEQ ID:13701, and is provided hereinbelow with reference to the sequence listing part.

[7126] VGAM512 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM512 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM512 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7127] VGAM512 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM512 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM512 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM512 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM512 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7128] The complementary binding of VGAM512 RNA, herein designated VGAM RNA, to host target binding sites on VGAM512 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM512 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM512 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7129] It is appreciated that VGAM512 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM512 host target genes. The mRNA of each one of this plurality of VGAM512 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM512 RNA, herein designated VGAM RNA, and which when bound by VGAM512 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM512 host target proteins.

[7130] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM512 gene, herein designated VGAM GENE, on one or more VGAM512 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7131] It is yet further appreciated that a function of VGAM512 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM512 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM512 correlate with, and may be deduced from, the identity of the host target genes which VGAM512 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7132] Nucleotide sequences of the VGAM512 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM512 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM512 are further described hereinbelow with reference to Table 1.

[7133] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM512 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7134] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 513 (VGAM513) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7135] VGAM513 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM513 was detected is described hereinabove with reference to Figs. 2-8.

[7136] VGAM513 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1.

VGAM513 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7137] VGAM513 gene, herein designated VGAM GENE, encodes a VGAM513 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM513 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM513 precursor RNA is designated SEQ ID:13705, and is provided hereinbelow with reference to the sequence listing part.

[7138] VGAM513 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM513 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7139] An enzyme complex designated DICER COMPLEX, dices

the VGAM513 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM513 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM513 RNA is designated SEQ ID:13706, and is provided hereinbelow with reference to the sequence listing part.

[7140] VGAM513 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM513 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM513 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7141] VGAM513 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM513 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM513 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM513 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM513 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7142] The complementary binding of VGAM513 RNA, herein designated VGAM RNA, to host target binding sites on VGAM513 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and



BINDING SITE III, inhibits translation of VGAM513 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM513 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7143] It is appreciated that VGAM513 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM513 host target genes. The mRNA of each one of this plurality of VGAM513 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM513 RNA, herein designated VGAM RNA, and which when bound by VGAM513 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM513 host target proteins.

[7144] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM513 gene, herein designated VGAM GENE, on one or more VGAM513 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7145] It is yet further appreciated that a function of VGAM513 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM513 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM513 correlate with, and may be deduced from, the identity of the host target genes which VGAM513 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7146] Nucleotide sequences of the VGAM513 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM513 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM513 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM513 are further described hereinbelow with reference to Table 1.

[7147] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM513 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7148] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 514 (VGAM514) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7149] VGAM514 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM514 was detected is described hereinabove with reference to Figs. 2-8.

[7150] VGAM514 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM514 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[7151] VGAM514 gene, herein designated VGAM GENE, encodes a VGAM514 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM514 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM514 precursor RNA is designated SEQ ID:13728, and is provided hereinbelow with reference to the sequence listing part.

[7152] VGAM514 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7153] An enzyme complex designated DICER COMPLEX, dices the VGAM514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM514 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM514 RNA is designated SEQ ID:13729, and is provided hereinbelow with reference to the sequence listing part.

[7154] VGAM514 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM514 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM514 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7155] VGAM514 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM514 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM514 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM514 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM514 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7156] The complementary binding of VGAM514 RNA, herein designated VGAM RNA, to host target binding sites on VGAM514 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM514 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM514 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7157] It is appreciated that VGAM514 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM514 host target genes. The mRNA of each one of this plurality of VGAM514 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM514 RNA, herein designated VGAM

RNA, and which when bound by VGAM514 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM514 host target proteins.

[7158] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM514 gene, herein designated VGAM GENE, on one or more VGAM514 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7159] It is yet further appreciated that a function of VGAM514 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM514 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM514 correlate with, and may be deduced from, the identity of the host target genes which VGAM514 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7160] Nucleotide sequences of the VGAM514 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM514 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM514 are further described hereinbelow with reference to Table 1.

[7161] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM514 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7162] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 515 (VGAM515) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7163] VGAM515 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM515 was detected is described hereinabove with reference to Figs. 2–8.

[7164] VGAM515 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 19. VGAM515 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7165] VGAM515 gene, herein designated VGAM GENE, encodes a VGAM515 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM515 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM515 precursor RNA is designated SEQ ID:13737, and is provided hereinbelow with reference to the sequence listing part.

[7166] VGAM515 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7167] An enzyme complex designated DICER COMPLEX, dices the VGAM515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM515 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM515 RNA is designated SEQ ID:13738, and is provided hereinbelow with reference to the sequence listing part.

[7168] VGAM515 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM515 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM515 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7169] VGAM515 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM515 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM515 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM515 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM515 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7170] The complementary binding of VGAM515 RNA, herein designated VGAM RNA, to host target binding sites on VGAM515 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM515 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM515 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7171] It is appreciated that VGAM515 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM515 host target genes. The mRNA of each one of this plurality of VGAM515 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM515 RNA, herein designated VGAM RNA, and which when bound by VGAM515 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM515 host target proteins.

[7172] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM515 gene, herein designated VGAM GENE, on one or more VGAM515 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7173] It is yet further appreciated that a function of VGAM515 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM515 include diagnosis, prevention and

treatment of viral infection by Human papillomavirus type 19. Specific functions, and accordingly utilities, of VGAM515 correlate with, and may be deduced from, the identity of the host target genes which VGAM515 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7174] Nucleotide sequences of the VGAM515 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM515 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM515 are further described hereinbelow with reference to Table 1.

[7175] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM515 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7176] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 516 (VGAM516) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7177] VGAM516 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM516 was detected is described hereinabove with reference to Figs. 2–8.

[7178] VGAM516 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 19. VGAM516 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7179] VGAM516 gene, herein designated VGAM GENE, encodes a VGAM516 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM516 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM516 precursor RNA is designated SEQ ID:13748, and is provided hereinbelow with reference to the sequence listing part.

[7180] VGAM516 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM516 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7181] An enzyme complex designated DICER COMPLEX, dices the VGAM516 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM516 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM516 RNA is designated SEQ ID:13749, and is provided hereinbelow with reference to the sequence listing part.

[7182] VGAM516 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM516 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM516 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7183] VGAM516 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM516 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM516 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM516 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM516 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7184] The complementary binding of VGAM516 RNA, herein designated VGAM RNA, to host target binding sites on VGAM516 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM516 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM516 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7185] It is appreciated that VGAM516 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM516 host target genes. The mRNA of each one of this plurality of VGAM516 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM516 RNA, herein designated VGAM RNA, and which when bound by VGAM516 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM516 host target proteins.

[7186] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM516 gene, herein designated VGAM GENE, on one or more VGAM516 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7187] It is yet further appreciated that a function of VGAM516 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM516 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type

19. Specific functions, and accordingly utilities, of VGAM516 correlate with, and may be deduced from, the identity of the host target genes which VGAM516 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7188] Nucleotide sequences of the VGAM516 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM516 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM516 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM516 are further described hereinbelow with reference to Table 1.

[7189] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM516 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7190] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 517 (VGAM517) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[7191] VGAM517 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM517 was detected is described hereinabove with reference to Figs. 2–8.

[7192] VGAM517 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 19. VGAM517 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7193] VGAM517 gene, herein designated VGAM GENE, encodes a VGAM517 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM517 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM517 precursor RNA is designated SEQ ID:13756, and is provided hereinbelow with reference to the sequence listing part.

[7194] VGAM517 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM517 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7195] An enzyme complex designated DICER COMPLEX, dices the VGAM517 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM517 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM517 RNA is designated SEQ ID:13757, and is provided hereinbelow with reference to the sequence listing part.

[7196] VGAM517 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM517 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM517 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7197] VGAM517 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM517 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM517 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM517 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM517 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7198] The complementary binding of VGAM517 RNA, herein designated VGAM RNA, to host target binding sites on VGAM517 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM517 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM517 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7199] It is appreciated that VGAM517 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM517 host target genes. The mRNA of each one of this plurality of VGAM517 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM517 RNA, herein designated VGAM RNA, and which when bound by VGAM517 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM517 host target proteins.

[7200] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM517 gene, herein designated VGAM GENE, on one or more VGAM517 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7201] It is yet further appreciated that a function of VGAM517 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM517 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 19. Specific functions, and accordingly utilities, of

VGAM517 correlate with, and may be deduced from, the identity of the host target genes which VGAM517 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7202] Nucleotide sequences of the VGAM517 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM517 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM517 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM517 are further described hereinbelow with reference to Table 1.

[7203] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM517 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7204] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 518 (VGAM518) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[7205] VGAM518 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM518 was detected is described hereinabove with reference to Figs. 2–8.

[7206] VGAM518 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM518 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7207] VGAM518 gene, herein designated VGAM GENE, encodes a VGAM518 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM518 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM518 precursor RNA is designated SEQ ID:13764, and is provided hereinbelow with reference to the sequence listing part.

[7208] VGAM518 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM518 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7209] An enzyme complex designated DICER COMPLEX, dices the VGAM518 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM518 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM518 RNA is designated SEQ ID:13765, and is provided hereinbelow with reference to the sequence listing part.

[7210] VGAM518 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM518 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM518 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7211] VGAM518 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM518 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM518 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM518 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM518 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7212] The complementary binding of VGAM518 RNA, herein designated VGAM RNA, to host target binding sites on VGAM518 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM518 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM518 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7213] It is appreciated that VGAM518 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM518 host target genes. The mRNA of each one of this plurality of VGAM518 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM518 RNA, herein designated VGAM RNA, and which when bound by VGAM518 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM518 host target proteins.

[7214] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM518 gene, herein designated VGAM GENE, on one or more VGAM518 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7215] It is yet further appreciated that a function of VGAM518 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM518 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM518 correlate with, and may be deduced from, the identity of the host



target genes which VGAM518 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7216] Nucleotide sequences of the VGAM518 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM518 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM518 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM518 are further described hereinbelow with reference to Table 1.

[7217] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM518 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7218] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 519 (VGAM519) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7219] VGAM519 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM519 was detected is described hereinabove with reference to Figs. 2–8.

[7220] VGAM519 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Euprosterna elaeasa virus. VGAM519 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7221] VGAM519 gene, herein designated VGAM GENE, encodes a VGAM519 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM519 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM519 precursor RNA is designated SEQ ID:13781, and is provided hereinbelow with reference to the sequence listing part.

[7222] VGAM519 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM519 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7223] An enzyme complex designated DICER COMPLEX, dices the VGAM519 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM519 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM519 RNA is designated SEQ ID:13782, and is provided hereinbelow with reference to the sequence listing part.

[7224] VGAM519 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM519 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM519 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7225] VGAM519 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM519 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM519 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM519 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM519 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7226] The complementary binding of VGAM519 RNA, herein designated VGAM RNA, to host target binding sites on VGAM519 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM519 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM519 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7227] It is appreciated that VGAM519 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM519 host target genes. The mRNA of each one of this plurality of VGAM519 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM519 RNA, herein designated VGAM RNA, and which when bound by VGAM519 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM519 host target proteins.

[7228] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM519 gene, herein designated VGAM GENE, on one or more VGAM519 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7229] It is yet further appreciated that a function of VGAM519 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM519 include diagnosis, prevention and treatment of viral infection by Euprosterna elaeasa virus. Specific functions, and accordingly utilities, of VGAM519 correlate with, and may be deduced from, the identity of the host target genes which VGAM519 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[7230] Nucleotide sequences of the VGAM519 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM519 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM519 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM519 are further described hereinbelow with reference to Table 1.

[7231] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM519 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7232] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 520 (VGAM520) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7233] VGAM520 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM520 was detected is described hereinabove with reference to Figs. 2–8.

[7234] VGAM520 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Euprosterna elaeasa virus. VGAM520 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7235] VGAM520 gene, herein designated VGAM GENE, encodes a VGAM520 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM520 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM520 precursor RNA is designated SEQ ID:13789, and is provided hereinbelow with reference to the sequence listing part.

[7236] VGAM520 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM520 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the



fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7237] An enzyme complex designated DICER COMPLEX, dices the VGAM520 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM520 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM520 RNA is designated SEQ ID:13790, and is provided hereinbelow with reference to the sequence listing part.

[7238] VGAM520 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM520 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM520 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7239] VGAM520 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM520 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM520 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM520 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM520 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[7240] The complementary binding of VGAM520 RNA, herein designated VGAM RNA, to host target binding sites on VGAM520 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM520 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM520 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7241] It is appreciated that VGAM520 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM520 host target genes. The mRNA of each one of this plurality of VGAM520 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM520 RNA, herein designated VGAM RNA, and which when bound by VGAM520 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM520 host target proteins.

[7242] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM520 gene, herein designated VGAM GENE, on one or more VGAM520 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7243] It is yet further appreciated that a function of VGAM520 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM520 include diagnosis, prevention and treatment of viral infection by Euprosterna elaeasa virus. Specific functions, and accordingly utilities, of VGAM520 correlate with, and may be deduced from, the identity of the host target genes which VGAM520 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[7244] Nucleotide sequences of the VGAM520 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM520 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM520 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM520 are further described hereinbelow with reference to Table 1.

[7245] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM520 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7246] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 521 (VGAM521) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7247] VGAM521 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM521 was detected is described hereinabove with reference to Figs. 2–8.

[7248] VGAM521 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Euprosterna elaeasa virus. VGAM521 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7249] VGAM521 gene, herein designated VGAM GENE, encodes a VGAM521 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM521 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM521 precursor RNA is designated SEQ ID:13827, and is provided hereinbelow with reference to the sequence listing part.

[7250] VGAM521 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM521 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7251] An enzyme complex designated DICER COMPLEX, dices the VGAM521 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM521 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM521 RNA is designated SEQ ID:13828, and is provided hereinbelow with reference to the sequence listing part.

[7252] VGAM521 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM521 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM521 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[7253] VGAM521 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM521 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM521 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM521 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM521 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[7254] The complementary binding of VGAM521 RNA, herein designated VGAM RNA, to host target binding sites on VGAM521 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM521 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM521 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7255] It is appreciated that VGAM521 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM521 host target genes. The mRNA of each one of this plurality of VGAM521 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM521 RNA, herein designated VGAM RNA, and which when bound by VGAM521 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM521 host target proteins.

[7256] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM521 gene, herein designated VGAM GENE, on one or

more VGAM521 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7257] It is yet further appreciated that a function of VGAM521 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM521 include diagnosis, prevention and treatment of viral infection by Euprosterna elaeasa virus. Specific functions, and accordingly utilities, of VGAM521 correlate with, and may be deduced from, the identity of the host target genes which VGAM521 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7258] Nucleotide sequences of the VGAM521 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM521 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM521 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM521 are further described hereinbelow with reference to Table 1.

[7259] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM521 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7260] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 522 (VGAM522) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7261] VGAM522 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM522 was detected is described

hereinabove with reference to Figs. 2–8.

[7262] VGAM522 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Euprosterna elaeasa virus. VGAM522 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7263] VGAM522 gene, herein designated VGAM GENE, encodes a VGAM522 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM522 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM522 precursor RNA is designated SEQ ID:13912, and is provided hereinbelow with reference to the sequence listing part.

[7264] VGAM522 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM522 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7265] An enzyme complex designated DICER COMPLEX, dices the VGAM522 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM522 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM522 RNA is designated SEQ ID:13913, and is provided hereinbelow with reference to the sequence listing part.

[7266] VGAM522 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM522 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM522 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7267] VGAM522 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM522 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM522 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM522 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM522 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7268] The complementary binding of VGAM522 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM522 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM522 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM522 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7269] It is appreciated that VGAM522 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM522 host target genes. The mRNA of each one of this plurality of VGAM522 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM522 RNA, herein designated VGAM RNA, and which when bound by VGAM522 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM522 host target proteins.

[7270] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM522 gene, herein designated VGAM GENE, on one or more VGAM522 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7271] It is yet further appreciated that a function of VGAM522 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM522 include diagnosis, prevention and treatment of viral infection by Euprosterna elaeasa virus. Specific functions, and accordingly utilities, of VGAM522 correlate with, and may be deduced from, the identity of the host target genes which VGAM522 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7272] Nucleotide sequences of the VGAM522 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM522 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM522 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM522 are further described hereinbelow with reference to Table 1.

[7273] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM522 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7274] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 523 (VGAM523) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7275] VGAM523 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM523 was detected is described hereinabove with reference to Figs. 2-8.

[7276] VGAM523 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Euprosterna elaeasa virus. VGAM523 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7277] VGAM523 gene, herein designated VGAM GENE, encodes a VGAM523 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM523 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM523 precursor RNA is designated SEQ ID:13923, and is provided hereinbelow with reference to the sequence listing part.

[7278] VGAM523 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM523 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[7279] An enzyme complex designated DICER COMPLEX, dices the VGAM523 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM523 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM523 RNA is designated SEQ ID:13924, and is provided hereinbelow with reference to the sequence listing part.

[7280] VGAM523 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM523 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM523 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7281] VGAM523 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM523 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM523 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM523 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM523 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7282] The complementary binding of VGAM523 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM523 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM523 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM523 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7283] It is appreciated that VGAM523 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM523 host target genes. The mRNA of each one of this plurality of VGAM523 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM523 RNA, herein designated VGAM RNA, and which when bound by VGAM523 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM523 host target proteins.

[7284] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM523 gene, herein designated VGAM GENE, on one or more VGAM523 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7285] It is yet further appreciated that a function of VGAM523 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM523 include diagnosis, prevention and treatment of viral infection by Euprosterna elaeasa virus. Specific functions, and accordingly utilities, of VGAM523 correlate with, and may be deduced from, the identity of the host target genes which VGAM523 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7286] Nucleotide sequences of the VGAM523 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM523 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM523 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM523 are further described hereinbelow with reference to Table 1.

[7287] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM523 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7288] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 524 (VGAM524) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7289] VGAM524 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM524 was detected is described hereinabove with reference to Figs. 2-8.

[7290] VGAM524 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Paramecium bursaria* Chlorella virus 1. VGAM524 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7291] VGAM524 gene, herein designated VGAM GENE, encodes a VGAM524 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM524 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM524 precursor RNA is designated SEQ ID:13934, and is provided hereinbelow with reference to the sequence listing part.

[7292] VGAM524 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM524 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[7293] An enzyme complex designated DICER COMPLEX, dices the VGAM524 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM524 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM524 RNA is designated SEQ ID:13935, and is provided hereinbelow with reference to the sequence listing part.

[7294] VGAM524 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM524 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM524 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7295] VGAM524 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM524 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM524 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM524 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM524 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7296] The complementary binding of VGAM524 RNA, herein designated VGAM RNA, to host target binding sites on VGAM524 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM524 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM524 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7297] It is appreciated that VGAM524 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM524 host target genes. The mRNA of each one of this plurality of VGAM524 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM524 RNA, herein designated VGAM RNA, and which when bound by VGAM524 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM524 host target proteins.

[7298] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM524 gene, herein designated VGAM GENE, on one or more VGAM524 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7299] It is yet further appreciated that a function of VGAM524 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM524 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM524 correlate with, and may be deduced from, the identity of the host target genes which VGAM524 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7300] Nucleotide sequences of the VGAM524 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM524 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM524 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM524 are further described hereinbelow with reference to Table 1.

[7301] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM524 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7302] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 525 (VGAM525) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7303] VGAM525 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM525 was detected is described hereinabove with reference to Figs. 2-8.

[7304] VGAM525 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria

Chlorella virus 1. VGAM525 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7305] VGAM525 gene, herein designated VGAM GENE, encodes a VGAM525 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM525 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM525 precursor RNA is designated SEQ ID:13951, and is provided hereinbelow with reference to the sequence listing part.

[7306] VGAM525 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM525 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7307] An enzyme complex designated DICER COMPLEX, dices

the VGAM525 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM525 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM525 RNA is designated SEQ ID:13952, and is provided hereinbelow with reference to the sequence listing part.

[7308] VGAM525 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM525 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM525 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7309] VGAM525 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM525 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM525 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM525 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM525 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7310] The complementary binding of VGAM525 RNA, herein designated VGAM RNA, to host target binding sites on VGAM525 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and



BINDING SITE III, inhibits translation of VGAM525 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM525 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7311] It is appreciated that VGAM525 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM525 host target genes. The mRNA of each one of this plurality of VGAM525 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM525 RNA, herein designated VGAM RNA, and which when bound by VGAM525 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM525 host target proteins.

[7312] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM525 gene, herein designated VGAM GENE, on one or more VGAM525 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7313] It is yet further appreciated that a function of VGAM525 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM525 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM525 correlate with, and may be deduced from, the identity of the host target genes which VGAM525 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7314] Nucleotide sequences of the VGAM525 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM525 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM525 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM525 are further described hereinbelow with reference to Table 1.

[7315] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM525 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7316] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 526 (VGAM526) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7317] VGAM526 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM526 was detected is described hereinabove with reference to Figs. 2-8.

[7318] VGAM526 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM526 host target gene, herein des-

ignated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7319] VGAM526 gene, herein designated VGAM GENE, encodes a VGAM526 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM526 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM526 precursor RNA is designated SEQ ID:13958, and is provided hereinbelow with reference to the sequence listing part.

[7320] VGAM526 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM526 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7321] An enzyme complex designated DICER COMPLEX, dices the VGAM526 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM526 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM526 RNA is designated SEQ ID:13959, and is provided hereinbelow with reference to the sequence listing part.

[7322] VGAM526 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM526 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM526 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7323] VGAM526 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM526 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM526 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM526 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM526 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7324] The complementary binding of VGAM526 RNA, herein designated VGAM RNA, to host target binding sites on VGAM526 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM526 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM526 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7325] It is appreciated that VGAM526 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM526 host target genes. The mRNA of each one of this plurality of VGAM526 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM526 RNA, herein designated VGAM RNA, and which when bound by VGAM526 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM526 host target proteins.

[7326] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM526 gene, herein designated VGAM GENE, on one or more VGAM526 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7327] It is yet further appreciated that a function of VGAM526 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM526 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM526 correlate with, and may be deduced from, the identity of the host target genes which VGAM526 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7328] Nucleotide sequences of the VGAM526 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM526 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM526 folded precursor RNA, herein designated VGAM



FOLDED PRECURSOR RNA, of VGAM526 are further described hereinbelow with reference to Table 1.

[7329] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM526 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7330] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 527 (VGAM527) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7331] VGAM527 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM527 was detected is described hereinabove with reference to Figs. 2-8.

[7332] VGAM527 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM527 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[7333] VGAM527 gene, herein designated VGAM GENE, encodes a VGAM527 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM527 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM527 precursor RNA is designated SEQ ID:13962, and is provided hereinbelow with reference to the sequence listing part.

[7334] VGAM527 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM527 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7335] An enzyme complex designated DICER COMPLEX, dices the VGAM527 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM527 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM527 RNA is designated SEQ ID:13963, and is provided hereinbelow with reference to the sequence listing part.

[7336] VGAM527 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM527 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM527 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7337] VGAM527 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM527 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM527 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM527 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM527 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7338] The complementary binding of VGAM527 RNA, herein designated VGAM RNA, to host target binding sites on VGAM527 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM527 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM527 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7339] It is appreciated that VGAM527 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM527 host target genes. The mRNA of each one of this plurality of VGAM527 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM527 RNA, herein designated VGAM RNA, and which when bound by VGAM527 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM527 host target proteins.

[7340] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM527 gene, herein designated VGAM GENE, on one or more VGAM527 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7341] It is yet further appreciated that a function of VGAM527 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM527 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM527 correlate with, and may be deduced from, the identity of the host target genes which VGAM527 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7342] Nucleotide sequences of the VGAM527 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM527 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM527 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM527 are further de-

scribed hereinbelow with reference to Table 1.

[7343] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM527 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7344] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 528 (VGAM528) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7345] VGAM528 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM528 was detected is described hereinabove with reference to Figs. 2-8.

[7346] VGAM528 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine oral papillomavirus. VGAM528 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7347] VGAM528 gene, herein designated VGAM GENE, encodes a VGAM528 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM528 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM528 precursor RNA is designated SEQ ID:13997, and is provided hereinbelow with reference to the sequence listing part.

[7348] VGAM528 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM528 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7349] An enzyme complex designated DICER COMPLEX, dices the VGAM528 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM528 RNA, herein designated VGAM RNA, a single stranded ~22 nt



long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM528 RNA is designated SEQ ID:13998, and is provided hereinbelow with reference to the sequence listing part.

[7350] VGAM528 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM528 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM528 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7351] VGAM528 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM528 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM528 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM528 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM528 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7352] The complementary binding of VGAM528 RNA, herein designated VGAM RNA, to host target binding sites on VGAM528 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM528 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM528 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7353] It is appreciated that VGAM528 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM528 host target genes. The mRNA of each one of this plurality of VGAM528 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM528 RNA, herein designated VGAM RNA, and which when bound by VGAM528 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM528 host target proteins.

[7354] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM528 gene, herein designated VGAM GENE, on one or more VGAM528 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7355] It is yet further appreciated that a function of VGAM528 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM528 include diagnosis, prevention and treatment of viral infection by Canine oral papillomavirus. Specific functions, and accordingly utilities, of VGAM528 correlate with, and may be deduced from, the identity of the host target genes which VGAM528 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7356] Nucleotide sequences of the VGAM528 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM528 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM528 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM528 are further described hereinbelow with reference to Table 1.

[7357] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM528 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7358] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 529 (VGAM529) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7359] VGAM529 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM529 was detected is described hereinabove with reference to Figs. 2-8.

[7360] VGAM529 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine oral papillomavirus. VGAM529 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7361] VGAM529 gene, herein designated VGAM GENE, encodes a

VGAM529 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM529 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM529 precursor RNA is designated SEQ ID:14033, and is provided hereinbelow with reference to the sequence listing part.

[7362] VGAM529 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM529 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7363] An enzyme complex designated DICER COMPLEX, dices the VGAM529 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM529 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM529 RNA is designated SEQ ID:14034, and is provided hereinbelow with reference to the sequence listing part.

[7364] VGAM529 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM529 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM529 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7365] VGAM529 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM529 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM529 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM529 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM529 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7366] The complementary binding of VGAM529 RNA, herein designated VGAM RNA, to host target binding sites on VGAM529 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM529 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM529 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein



is therefore outlined by a broken line.

[7367] It is appreciated that VGAM529 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM529 host target genes. The mRNA of each one of this plurality of VGAM529 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM529 RNA, herein designated VGAM RNA, and which when bound by VGAM529 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM529 host target proteins.

[7368] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM529 gene, herein designated VGAM GENE, on one or more VGAM529 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7369] It is yet further appreciated that a function of VGAM529 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM529 include diagnosis, prevention and treatment of viral infection by Canine oral papillomavirus. Specific functions, and accordingly utilities, of VGAM529 correlate with, and may be deduced from, the identity of the host target genes which VGAM529 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7370] Nucleotide sequences of the VGAM529 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM529 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM529 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM529 are further described hereinbelow with reference to Table 1.

[7371] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM529 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7372] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 530 (VGAM530) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7373] VGAM530 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM530 was detected is described hereinabove with reference to Figs. 2-8.

[7374] VGAM530 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM530 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7375] VGAM530 gene, herein designated VGAM GENE, encodes a VGAM530 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM530 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM530 precursor RNA is designated SEQ ID:14046, and is provided hereinbelow with reference to the sequence listing part.

[7376] VGAM530 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM530 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7377] An enzyme complex designated DICER COMPLEX, dices the VGAM530 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM530 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM530 RNA is designated SEQ ID:14047, and is provided hereinbelow with reference to the sequence listing part.

[7378] VGAM530 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM530 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM530 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7379] VGAM530 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM530 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM530 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM530 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM530 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7380] The complementary binding of VGAM530 RNA, herein designated VGAM RNA, to host target binding sites on VGAM530 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM530 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM530 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7381] It is appreciated that VGAM530 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM530 host target genes. The mRNA of each one of this plurality of VGAM530 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM530 RNA, herein designated VGAM RNA, and which when bound by VGAM530 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM530 host target proteins.

[7382] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM530 gene, herein designated VGAM GENE, on one or more VGAM530 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7383] It is yet further appreciated that a function of VGAM530 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM530 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM530 correlate with, and may be deduced from, the identity of the host target genes which VGAM530 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7384] Nucleotide sequences of the VGAM530 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM530 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM530 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM530 are further described hereinbelow with reference to Table 1.

[7385] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of



Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM530 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7386] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 531 (VGAM531) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7387] VGAM531 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM531 was detected is described hereinabove with reference to Figs. 2–8.

[7388] VGAM531 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Little cherry virus.

VGAM531 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7389] VGAM531 gene, herein designated VGAM GENE, encodes a VGAM531 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM531 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM531 precursor RNA is designated SEQ ID:14058, and is provided hereinbelow with reference to the sequence listing part.

[7390] VGAM531 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM531 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7391] An enzyme complex designated DICER COMPLEX, dices the VGAM531 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM531 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM531 RNA is designated SEQ ID:14059, and is provided hereinbelow with reference to the sequence listing part.

[7392] VGAM531 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM531 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM531 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7393] VGAM531 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM531 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM531 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM531 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM531 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7394] The complementary binding of VGAM531 RNA, herein designated VGAM RNA, to host target binding sites on VGAM531 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM531 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM531 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7395] It is appreciated that VGAM531 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM531 host target genes. The mRNA of each one of this plurality of VGAM531 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM531 RNA, herein designated VGAM RNA, and which when bound by VGAM531 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM531 host target proteins.

[7396] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM531 gene, herein designated VGAM GENE, on one or more VGAM531 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7397] It is yet further appreciated that a function of VGAM531 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM531 include diagnosis, prevention and treatment of viral infection by Little cherry virus. Specific functions, and accordingly utilities, of VGAM531 correlate with, and may be deduced from, the identity of the host target genes which VGAM531 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7398] Nucleotide sequences of the VGAM531 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM531 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM531 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM531 are further described hereinbelow with reference to Table 1.

[7399] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM531 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7400] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 532 (VGAM532) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7401] VGAM532 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM532 was detected is described hereinabove with reference to Figs. 2–8.

[7402] VGAM532 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Reston Ebola virus. VGAM532 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7403] VGAM532 gene, herein designated VGAM GENE, encodes a VGAM532 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM532 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM532 precursor RNA is designated SEQ ID:14064, and is provided hereinbelow with reference to the sequence listing part.

[7404] VGAM532 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM532 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7405] An enzyme complex designated DICER COMPLEX, dices the VGAM532 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM532 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other



necessary proteins. A probable (over 55%) nucleotide sequence of VGAM532 RNA is designated SEQ ID:14065, and is provided hereinbelow with reference to the sequence listing part.

[7406] VGAM532 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM532 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM532 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7407] VGAM532 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM532 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM532 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM532 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM532 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7408] The complementary binding of VGAM532 RNA, herein designated VGAM RNA, to host target binding sites on VGAM532 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM532 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM532 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7409] It is appreciated that VGAM532 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM532 host target genes. The mRNA of each one of this plurality of VGAM532 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM532 RNA, herein designated VGAM RNA, and which when bound by VGAM532 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM532 host target proteins.

[7410] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM532 gene, herein designated VGAM GENE, on one or more VGAM532 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[7411] It is yet further appreciated that a function of VGAM532 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM532 include diagnosis, prevention and treatment of viral infection by Reston Ebola virus. Specific functions, and accordingly utilities, of VGAM532 correlate with, and may be deduced from, the identity of the host target genes which VGAM532 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[7412] Nucleotide sequences of the VGAM532 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM532 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM532 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM532 are further described hereinbelow with reference to Table 1.

[7413] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM532 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7414] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 533 (VGAM533) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7415] VGAM533 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM533 was detected is described hereinabove with reference to Figs. 2–8.

[7416] VGAM533 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Reston Ebola virus. VGAM533 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7417] VGAM533 gene, herein designated VGAM GENE, encodes a VGAM533 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM533 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM533 precursor RNA is designated SEQ ID:14073, and is provided hereinbelow with reference to the sequence listing part.

[7418] VGAM533 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM533 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7419] An enzyme complex designated DICER COMPLEX, dices the VGAM533 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM533 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM533 RNA is designated SEQ ID:14074, and is provided hereinbelow with reference to the sequence listing part.

[7420] VGAM533 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM533 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM533 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7421] VGAM533 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM533 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM533 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM533 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM533 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7422] The complementary binding of VGAM533 RNA, herein designated VGAM RNA, to host target binding sites on VGAM533 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM533 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM533 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7423] It is appreciated that VGAM533 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM533 host target genes. The mRNA of



each one of this plurality of VGAM533 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM533 RNA, herein designated VGAM RNA, and which when bound by VGAM533 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM533 host target proteins.

[7424] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM533 gene, herein designated VGAM GENE, on one or more VGAM533 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[7425] It is yet further appreciated that a function of VGAM533 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM533 include diagnosis, prevention and treatment of viral infection by Reston Ebola virus. Specific functions, and accordingly utilities, of VGAM533 correlate with, and may be deduced from, the identity of the host target genes which VGAM533 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[7426] Nucleotide sequences of the VGAM533 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM533 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM533 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM533 are further described hereinbelow with reference to Table 1.

[7427] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM533 RNA, herein designated VGAM RNA, are de—

scribed hereinbelow with reference to Table 2.

[7428] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 534 (VGAM534) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7429] VGAM534 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM534 was detected is described hereinabove with reference to Figs. 2–8.

[7430] VGAM534 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM534 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7431] VGAM534 gene, herein designated VGAM GENE, encodes a VGAM534 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM534 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM534 precursor RNA is designated SEQ ID:14079, and is provided hereinbelow with reference to the sequence listing part.

[7432] VGAM534 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM534 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7433] An enzyme complex designated DICER COMPLEX, dices the VGAM534 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM534 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM534 RNA is designated SEQ ID:14080, and

is provided hereinbelow with reference to the sequence listing part.

[7434] VGAM534 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM534 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM534 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7435] VGAM534 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM534 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM534 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM534 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM534 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7436] The complementary binding of VGAM534 RNA, herein designated VGAM RNA, to host target binding sites on VGAM534 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM534 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM534 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7437] It is appreciated that VGAM534 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM534 host target genes. The mRNA of each one of this plurality of VGAM534 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM534 RNA, herein designated VGAM RNA, and which when bound by VGAM534 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM534 host target proteins.

[7438] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM534 gene, herein designated VGAM GENE, on one or more VGAM534 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7439] It is yet further appreciated that a function of VGAM534 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM534 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM534 correlate with, and may be deduced from, the identity of the host target genes which VGAM534 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7440] Nucleotide sequences of the VGAM534 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM534 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM534 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM534 are further described hereinbelow with reference to Table 1.

[7441] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM534 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.



[7442] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 535 (VGAM535) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7443] VGAM535 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM535 was detected is described hereinabove with reference to Figs. 2–8.

[7444] VGAM535 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM535 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7445] VGAM535 gene, herein designated VGAM GENE, encodes a VGAM535 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM535 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM535 precursor RNA is

designated SEQ ID:14105, and is provided hereinbelow with reference to the sequence listing part.

[7446] VGAM535 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM535 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7447] An enzyme complex designated DICER COMPLEX, dices the VGAM535 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM535 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM535 RNA is designated SEQ ID:14106, and is provided hereinbelow with reference to the sequence

listing part.

[7448] VGAM535 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM535 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM535 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7449] VGAM535 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM535 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM535 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM535 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM535 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7450] The complementary binding of VGAM535 RNA, herein designated VGAM RNA, to host target binding sites on VGAM535 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM535 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM535 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7451] It is appreciated that VGAM535 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM535 host target genes. The mRNA of each one of this plurality of VGAM535 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM535 RNA, herein designated VGAM RNA, and which when bound by VGAM535 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM535 host target proteins.

[7452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM535 gene, herein designated VGAM GENE, on one or more VGAM535 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7453] It is yet further appreciated that a function of VGAM535 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM535 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM535 correlate with, and may be deduced from, the identity of the host target genes which VGAM535 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7454] Nucleotide sequences of the VGAM535 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM535 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM535 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM535 are further described hereinbelow with reference to Table 1.

[7455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM535 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7456] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 536 (VGAM536) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7457] VGAM536 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM536 was detected is described hereinabove with reference to Figs. 2–8.

[7458] VGAM536 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM536 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7459] VGAM536 gene, herein designated VGAM GENE, encodes a VGAM536 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM536 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM536 precursor RNA is designated SEQ ID:14123, and is provided hereinbelow

with reference to the sequence listing part.

[7460] VGAM536 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM536 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7461] An enzyme complex designated DICER COMPLEX, dices the VGAM536 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM536 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM536 RNA is designated SEQ ID:14124, and is provided hereinbelow with reference to the sequence listing part.



[7462] VGAM536 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM536 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM536 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7463] VGAM536 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM536 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM536 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM536 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM536 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7464] The complementary binding of VGAM536 RNA, herein designated VGAM RNA, to host target binding sites on VGAM536 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM536 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM536 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7465] It is appreciated that VGAM536 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM536 host target genes. The mRNA of each one of this plurality of VGAM536 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM536 RNA, herein designated VGAM RNA, and which when bound by VGAM536 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM536 host target proteins.

[7466] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM536 gene, herein designated VGAM GENE, on one or more VGAM536 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7467] It is yet further appreciated that a function of VGAM536 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM536 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM536 correlate with, and may be deduced from, the identity of the host target genes which VGAM536 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7468] Nucleotide sequences of the VGAM536 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM536 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM536 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM536 are further described hereinbelow with reference to Table 1.

[7469] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM536 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7470] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 537 (VGAM537) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7471] VGAM537 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM537 was detected is described hereinabove with reference to Figs. 2–8.

[7472] VGAM537 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM537 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7473] VGAM537 gene, herein designated VGAM GENE, encodes a VGAM537 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM537 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM537 precursor RNA is designated SEQ ID:14130, and is provided hereinbelow with reference to the sequence listing part.

[7474] VGAM537 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM537 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7475] An enzyme complex designated DICER COMPLEX, dices the VGAM537 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM537 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM537 RNA is designated SEQ ID:14131, and is provided hereinbelow with reference to the sequence listing part.

[7476] VGAM537 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM537 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM537 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7477] VGAM537 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM537 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM537 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM537 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM537 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7478] The complementary binding of VGAM537 RNA, herein designated VGAM RNA, to host target binding sites on VGAM537 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM537 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM537 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7479] It is appreciated that VGAM537 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM537 host target genes. The mRNA of each one of this plurality of VGAM537 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM537 RNA, herein designated VGAM



RNA, and which when bound by VGAM537 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM537 host target proteins.

[7480] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM537 gene, herein designated VGAM GENE, on one or more VGAM537 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7481] It is yet further appreciated that a function of VGAM537 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM537 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM537 correlate with, and may be deduced from, the identity of the host target genes which VGAM537 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7482] Nucleotide sequences of the VGAM537 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM537 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM537 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM537 are further described hereinbelow with reference to Table 1.

[7483] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM537 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7484] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 538 (VGAM538) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7485] VGAM538 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM538 was detected is described hereinabove with reference to Figs. 2-8.

[7486] VGAM538 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human foamy virus. VGAM538 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7487] VGAM538 gene, herein designated VGAM GENE, encodes a VGAM538 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM538 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM538 precursor RNA is designated SEQ ID:14135, and is provided hereinbelow with reference to the sequence listing part.

[7488] VGAM538 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM538 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7489] An enzyme complex designated DICER COMPLEX, dices the VGAM538 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM538 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM538 RNA is designated SEQ ID:14136, and is provided hereinbelow with reference to the sequence listing part.

[7490] VGAM538 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM538 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM538 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7491] VGAM538 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM538 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM538 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM538 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM538 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7492] The complementary binding of VGAM538 RNA, herein designated VGAM RNA, to host target binding sites on VGAM538 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM538 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM538 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7493] It is appreciated that VGAM538 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM538 host target genes. The mRNA of each one of this plurality of VGAM538 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM538 RNA, herein designated VGAM RNA, and which when bound by VGAM538 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM538 host target proteins.

[7494] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM538 gene, herein designated VGAM GENE, on one or more VGAM538 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7495] It is yet further appreciated that a function of VGAM538 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM538 include diagnosis, prevention and

treatment of viral infection by Human foamy virus. Specific functions, and accordingly utilities, of VGAM538 correlate with, and may be deduced from, the identity of the host target genes which VGAM538 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7496] Nucleotide sequences of the VGAM538 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM538 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM538 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM538 are further described hereinbelow with reference to Table 1.

[7497] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM538 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7498] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 539 (VGAM539) viral gene, which modulates ex-



pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7499] VGAM539 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM539 was detected is described hereinabove with reference to Figs. 2–8.

[7500] VGAM539 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine adenovirus D. VGAM539 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7501] VGAM539 gene, herein designated VGAM GENE, encodes a VGAM539 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM539 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM539 precursor RNA is designated SEQ ID:14170, and is provided hereinbelow with reference to the sequence listing part.

[7502] VGAM539 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM539 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7503] An enzyme complex designated DICER COMPLEX, dices the VGAM539 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM539 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM539 RNA is designated SEQ ID:14171, and is provided hereinbelow with reference to the sequence listing part.

[7504] VGAM539 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM539 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM539 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7505] VGAM539 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM539 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM539 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM539 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM539 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7506] The complementary binding of VGAM539 RNA, herein designated VGAM RNA, to host target binding sites on VGAM539 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM539 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM539 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7507] It is appreciated that VGAM539 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM539 host target genes. The mRNA of each one of this plurality of VGAM539 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM539 RNA, herein designated VGAM RNA, and which when bound by VGAM539 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM539 host target proteins.

[7508] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM539 gene, herein designated VGAM GENE, on one or more VGAM539 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7509] It is yet further appreciated that a function of VGAM539 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM539 include diagnosis, prevention and treatment of viral infection by Bovine adenovirus D. Spe-

cific functions, and accordingly utilities, of VGAM539 correlate with, and may be deduced from, the identity of the host target genes which VGAM539 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7510] Nucleotide sequences of the VGAM539 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM539 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM539 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM539 are further described hereinbelow with reference to Table 1.

[7511] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM539 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7512] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 540 (VGAM540) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[7513] VGAM540 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM540 was detected is described hereinabove with reference to Figs. 2–8.

[7514] VGAM540 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine adenovirus D. VGAM540 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7515] VGAM540 gene, herein designated VGAM GENE, encodes a VGAM540 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM540 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM540 precursor RNA is designated SEQ ID:14185, and is provided hereinbelow with reference to the sequence listing part.

[7516] VGAM540 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM540 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7517] An enzyme complex designated DICER COMPLEX, dices the VGAM540 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM540 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM540 RNA is designated SEQ ID:14186, and is provided hereinbelow with reference to the sequence listing part.

[7518] VGAM540 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM540 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM540 host target RNA, herein



designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7519] VGAM540 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM540 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM540 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM540 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM540 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7520] The complementary binding of VGAM540 RNA, herein designated VGAM RNA, to host target binding sites on VGAM540 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM540 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM540 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7521] It is appreciated that VGAM540 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM540 host target genes. The mRNA of each one of this plurality of VGAM540 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM540 RNA, herein designated VGAM RNA, and which when bound by VGAM540 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM540 host target proteins.

[7522] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM540 gene, herein designated VGAM GENE, on one or more VGAM540 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7523] It is yet further appreciated that a function of VGAM540 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM540 include diagnosis, prevention and treatment of viral infection by Bovine adenovirus D. Specific functions, and accordingly utilities, of VGAM540 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM540 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7524] Nucleotide sequences of the VGAM540 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM540 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM540 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM540 are further described hereinbelow with reference to Table 1.

[7525] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM540 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7526] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 541 (VGAM541) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[7527] VGAM541 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM541 was detected is described hereinabove with reference to Figs. 2–8.

[7528] VGAM541 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human foamy virus. VGAM541 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7529] VGAM541 gene, herein designated VGAM GENE, encodes a VGAM541 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM541 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM541 precursor RNA is designated SEQ ID:14197, and is provided hereinbelow with reference to the sequence listing part.

[7530] VGAM541 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM541 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7531] An enzyme complex designated DICER COMPLEX, dices the VGAM541 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM541 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM541 RNA is designated SEQ ID:14198, and is provided hereinbelow with reference to the sequence listing part.

[7532] VGAM541 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM541 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM541 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7533] VGAM541 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM541 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM541 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM541 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM541 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7534] The complementary binding of VGAM541 RNA, herein designated VGAM RNA, to host target binding sites on VGAM541 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM541 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM541 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7535] It is appreciated that VGAM541 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM541 host target genes. The mRNA of each one of this plurality of VGAM541 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM541 RNA, herein designated VGAM RNA, and which when bound by VGAM541 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM541 host target proteins.

[7536] It is further appreciated by one skilled in the art that the



mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM541 gene, herein designated VGAM GENE, on one or more VGAM541 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7537] It is yet further appreciated that a function of VGAM541 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM541 include diagnosis, prevention and treatment of viral infection by Human foamy virus. Specific functions, and accordingly utilities, of VGAM541 correlate with, and may be deduced from, the identity of the host

target genes which VGAM541 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7538] Nucleotide sequences of the VGAM541 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM541 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM541 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM541 are further described hereinbelow with reference to Table 1.

[7539] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM541 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7540] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 542 (VGAM542) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7541] VGAM542 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM542 was detected is described hereinabove with reference to Figs. 2–8.

[7542] VGAM542 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human foamy virus. VGAM542 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7543] VGAM542 gene, herein designated VGAM GENE, encodes a VGAM542 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM542 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM542 precursor RNA is designated SEQ ID:14208, and is provided hereinbelow with reference to the sequence listing part.

[7544] VGAM542 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM542 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7545] An enzyme complex designated DICER COMPLEX, dices the VGAM542 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM542 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM542 RNA is designated SEQ ID:14209, and is provided hereinbelow with reference to the sequence listing part.

[7546] VGAM542 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM542 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM542 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7547] VGAM542 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM542 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM542 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM542 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM542 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7548] The complementary binding of VGAM542 RNA, herein designated VGAM RNA, to host target binding sites on VGAM542 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM542 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM542 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7549] It is appreciated that VGAM542 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM542 host target genes. The mRNA of each one of this plurality of VGAM542 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM542 RNA, herein designated VGAM RNA, and which when bound by VGAM542 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM542 host target proteins.

[7550] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM542 gene, herein designated VGAM GENE, on one or more VGAM542 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7551] It is yet further appreciated that a function of VGAM542 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM542 include diagnosis, prevention and treatment of viral infection by Human foamy virus. Specific functions, and accordingly utilities, of VGAM542 correlate with, and may be deduced from, the identity of the host target genes which VGAM542 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[7552] Nucleotide sequences of the VGAM542 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM542 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM542 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM542 are further described hereinbelow with reference to Table 1.

[7553] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM542 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7554] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 543 (VGAM543) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7555] VGAM543 is a novel bioinformatically detected regulatory,



non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM543 was detected is described hereinabove with reference to Figs. 2–8.

[7556] VGAM543 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine adenovirus D. VGAM543 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7557] VGAM543 gene, herein designated VGAM GENE, encodes a VGAM543 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM543 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM543 precursor RNA is designated SEQ ID:14215, and is provided hereinbelow with reference to the sequence listing part.

[7558] VGAM543 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM543 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7559] An enzyme complex designated DICER COMPLEX, dices the VGAM543 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM543 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM543 RNA is designated SEQ ID:14216, and is provided hereinbelow with reference to the sequence listing part.

[7560] VGAM543 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM543 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM543 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7561] VGAM543 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM543 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM543 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM543 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM543 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[7562] The complementary binding of VGAM543 RNA, herein designated VGAM RNA, to host target binding sites on VGAM543 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM543 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM543 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7563] It is appreciated that VGAM543 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM543 host target genes. The mRNA of each one of this plurality of VGAM543 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM543 RNA, herein designated VGAM RNA, and which when bound by VGAM543 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM543 host target proteins.

[7564] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM543 gene, herein designated VGAM GENE, on one or more VGAM543 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7565] It is yet further appreciated that a function of VGAM543 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM543 include diagnosis, prevention and treatment of viral infection by Bovine adenovirus D. Specific functions, and accordingly utilities, of VGAM543 correlate with, and may be deduced from, the identity of the host target genes which VGAM543 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[7566] Nucleotide sequences of the VGAM543 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM543 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM543 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM543 are further described hereinbelow with reference to Table 1.

[7567] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM543 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7568] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 544 (VGAM544) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7569] VGAM544 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM544 was detected is described hereinabove with reference to Figs. 2–8.

[7570] VGAM544 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM544 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7571] VGAM544 gene, herein designated VGAM GENE, encodes a VGAM544 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM544 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM544 precursor RNA is designated SEQ ID:14223, and is provided hereinbelow with reference to the sequence listing part.

[7572] VGAM544 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM544 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7573] An enzyme complex designated DICER COMPLEX, dices the VGAM544 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM544 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM544 RNA is designated SEQ ID:14224, and is provided hereinbelow with reference to the sequence listing part.

[7574] VGAM544 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM544 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM544 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and



3UTR respectively.

[7575] VGAM544 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM544 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM544 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM544 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM544 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7576] The complementary binding of VGAM544 RNA, herein designated VGAM RNA, to host target binding sites on VGAM544 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM544 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM544 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7577] It is appreciated that VGAM544 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM544 host target genes. The mRNA of each one of this plurality of VGAM544 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM544 RNA, herein designated VGAM RNA, and which when bound by VGAM544 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM544 host target proteins.

[7578] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM544 gene, herein designated VGAM GENE, on one or

more VGAM544 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7579] It is yet further appreciated that a function of VGAM544 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM544 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM544 correlate with, and may be deduced from, the identity of the host target genes which VGAM544 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7580] Nucleotide sequences of the VGAM544 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM544 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM544 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM544 are further described hereinbelow with reference to Table 1.

[7581] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM544 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7582] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 545 (VGAM545) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7583] VGAM545 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM545 was detected is described

hereinabove with reference to Figs. 2–8.

[7584] VGAM545 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Mouse mammary tumor virus. VGAM545 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7585] VGAM545 gene, herein designated VGAM GENE, encodes a VGAM545 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM545 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM545 precursor RNA is designated SEQ ID:14229, and is provided hereinbelow with reference to the sequence listing part.

[7586] VGAM545 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM545 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7587] An enzyme complex designated DICER COMPLEX, dices the VGAM545 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM545 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM545 RNA is designated SEQ ID:14230, and is provided hereinbelow with reference to the sequence listing part.

[7588] VGAM545 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM545 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM545 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7589] VGAM545 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM545 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM545 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM545 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM545 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7590] The complementary binding of VGAM545 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM545 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM545 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM545 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7591] It is appreciated that VGAM545 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM545 host target genes. The mRNA of each one of this plurality of VGAM545 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM545 RNA, herein designated VGAM RNA, and which when bound by VGAM545 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM545 host target proteins.

[7592] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM545 gene, herein designated VGAM GENE, on one or more VGAM545 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7593] It is yet further appreciated that a function of VGAM545 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM545 include diagnosis, prevention and treatment of viral infection by Mouse mammary tumor virus. Specific functions, and accordingly utilities, of VGAM545 correlate with, and may be deduced from, the identity of the host target genes which VGAM545 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7594] Nucleotide sequences of the VGAM545 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM545 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM545 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM545 are further described hereinbelow with reference to Table 1.

[7595] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM545 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7596] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 546 (VGAM546) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7597] VGAM546 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM546 was detected is described hereinabove with reference to Figs. 2-8.

[7598] VGAM546 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM546 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7599] VGAM546 gene, herein designated VGAM GENE, encodes a VGAM546 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM546 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM546 precursor RNA is designated SEQ ID:14251, and is provided hereinbelow with reference to the sequence listing part.

[7600] VGAM546 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM546 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[7601] An enzyme complex designated DICER COMPLEX, dices the VGAM546 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM546 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM546 RNA is designated SEQ ID:14252, and is provided hereinbelow with reference to the sequence listing part.

[7602] VGAM546 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM546 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM546 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7603] VGAM546 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM546 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM546 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM546 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM546 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7604] The complementary binding of VGAM546 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM546 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM546 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM546 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7605] It is appreciated that VGAM546 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM546 host target genes. The mRNA of each one of this plurality of VGAM546 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM546 RNA, herein designated VGAM RNA, and which when bound by VGAM546 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM546 host target proteins.

[7606] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM546 gene, herein designated VGAM GENE, on one or more VGAM546 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7607] It is yet further appreciated that a function of VGAM546 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM546 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM546 correlate with, and may be deduced from, the identity of the host target genes which VGAM546 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7608] Nucleotide sequences of the VGAM546 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM546 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM546 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM546 are further described hereinbelow with reference to Table 1.

[7609] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM546 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7610] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 547 (VGAM547) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7611] VGAM547 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM547 was detected is described hereinabove with reference to Figs. 2-8.

[7612] VGAM547 gene, herein designated VGAM GENE, is a viral



gene contained in the genome of Human herpesvirus 1. VGAM547 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7613] VGAM547 gene, herein designated VGAM GENE, encodes a VGAM547 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM547 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM547 precursor RNA is designated SEQ ID:14263, and is provided hereinbelow with reference to the sequence listing part.

[7614] VGAM547 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM547 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7615] An enzyme complex designated DICER COMPLEX, dices the VGAM547 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM547 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM547 RNA is designated SEQ ID:14264, and is provided hereinbelow with reference to the sequence listing part.

[7616] VGAM547 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM547 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM547 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7617] VGAM547 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM547 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM547 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM547 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM547 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7618] The complementary binding of VGAM547 RNA, herein designated VGAM RNA, to host target binding sites on VGAM547 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM547 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM547 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7619] It is appreciated that VGAM547 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM547 host target genes. The mRNA of each one of this plurality of VGAM547 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM547 RNA, herein designated VGAM RNA, and which when bound by VGAM547 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM547 host target proteins.

[7620] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM547 gene, herein designated VGAM GENE, on one or more VGAM547 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7621] It is yet further appreciated that a function of VGAM547 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM547 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM547 correlate with, and may be deduced from, the identity of the host target genes which VGAM547 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7622] Nucleotide sequences of the VGAM547 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM547 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM547 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM547 are further described hereinbelow with reference to Table 1.

[7623] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM547 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7624] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 548 (VGAM548) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7625] VGAM548 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM548 was detected is described hereinabove with reference to Figs. 2-8.

[7626] VGAM548 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Mouse mammary tumor

virus. VGAM548 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7627] VGAM548 gene, herein designated VGAM GENE, encodes a VGAM548 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM548 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM548 precursor RNA is designated SEQ ID:14266, and is provided hereinbelow with reference to the sequence listing part.

[7628] VGAM548 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM548 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7629] An enzyme complex designated DICER COMPLEX, dices

the VGAM548 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM548 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM548 RNA is designated SEQ ID:14267, and is provided hereinbelow with reference to the sequence listing part.

[7630] VGAM548 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM548 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM548 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7631] VGAM548 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM548 host target



RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM548 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM548 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM548 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7632] The complementary binding of VGAM548 RNA, herein designated VGAM RNA, to host target binding sites on VGAM548 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM548 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM548 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7633] It is appreciated that VGAM548 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM548 host target genes. The mRNA of each one of this plurality of VGAM548 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM548 RNA, herein designated VGAM RNA, and which when bound by VGAM548 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM548 host target proteins.

[7634] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM548 gene, herein designated VGAM GENE, on one or more VGAM548 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7635] It is yet further appreciated that a function of VGAM548 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM548 include diagnosis, prevention and treatment of viral infection by Mouse mammary tumor virus. Specific functions, and accordingly utilities, of VGAM548 correlate with, and may be deduced from, the identity of the host target genes which VGAM548 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7636] Nucleotide sequences of the VGAM548 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM548 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM548 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM548 are further described hereinbelow with reference to Table 1.

[7637] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM548 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7638] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 549 (VGAM549) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7639] VGAM549 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM549 was detected is described hereinabove with reference to Figs. 2-8.

[7640] VGAM549 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM549 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[7641] VGAM549 gene, herein designated VGAM GENE, encodes a VGAM549 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM549 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM549 precursor RNA is designated SEQ ID:14278, and is provided hereinbelow with reference to the sequence listing part.

[7642] VGAM549 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM549 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7643] An enzyme complex designated DICER COMPLEX, dices the VGAM549 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM549 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM549 RNA is designated SEQ ID:14279, and is provided hereinbelow with reference to the sequence listing part.

[7644] VGAM549 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM549 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM549 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7645] VGAM549 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM549 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM549 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM549 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM549 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7646] The complementary binding of VGAM549 RNA, herein designated VGAM RNA, to host target binding sites on VGAM549 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM549 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM549 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7647] It is appreciated that VGAM549 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM549 host target genes. The mRNA of each one of this plurality of VGAM549 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM549 RNA, herein designated VGAM RNA, and which when bound by VGAM549 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM549 host target proteins.

[7648] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM549 gene, herein designated VGAM GENE, on one or more VGAM549 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated



only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7649] It is yet further appreciated that a function of VGAM549 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM549 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM549 correlate with, and may be deduced from, the identity of the host target genes which VGAM549 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7650] Nucleotide sequences of the VGAM549 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM549 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM549 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM549 are further described hereinbelow with reference to Table 1.

[7651] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM549 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7652] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 550 (VGAM550) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7653] VGAM550 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM550 was detected is described hereinabove with reference to Figs. 2-8.

[7654] VGAM550 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM550 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[7655] VGAM550 gene, herein designated VGAM GENE, encodes a VGAM550 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM550 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM550 precursor RNA is designated SEQ ID:14431, and is provided hereinbelow with reference to the sequence listing part.

[7656] VGAM550 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM550 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7657] An enzyme complex designated DICER COMPLEX, dices the VGAM550 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM550 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM550 RNA is designated SEQ ID:14432, and is provided hereinbelow with reference to the sequence listing part.

[7658] VGAM550 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM550 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM550 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7659] VGAM550 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM550 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM550 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM550 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM550 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7660] The complementary binding of VGAM550 RNA, herein designated VGAM RNA, to host target binding sites on VGAM550 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM550 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM550 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7661] It is appreciated that VGAM550 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM550 host target genes. The mRNA of each one of this plurality of VGAM550 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM550 RNA, herein designated VGAM RNA, and which when bound by VGAM550 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM550 host target proteins.

[7662] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM550 gene, herein designated VGAM GENE, on one or more VGAM550 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7663] It is yet further appreciated that a function of VGAM550 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM550 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM550 correlate with, and may be deduced from, the identity of the host target genes which VGAM550 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7664] Nucleotide sequences of the VGAM550 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM550 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM550 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM550 are further de-

scribed hereinbelow with reference to Table 1.

[7665] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM550 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7666] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 551 (VGAM551) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7667] VGAM551 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM551 was detected is described hereinabove with reference to Figs. 2-8.

[7668] VGAM551 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM551 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.



[7669] VGAM551 gene, herein designated VGAM GENE, encodes a VGAM551 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM551 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM551 precursor RNA is designated SEQ ID:14437, and is provided hereinbelow with reference to the sequence listing part.

[7670] VGAM551 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM551 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7671] An enzyme complex designated DICER COMPLEX, dices the VGAM551 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM551 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM551 RNA is designated SEQ ID:14438, and is provided hereinbelow with reference to the sequence listing part.

[7672] VGAM551 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM551 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM551 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7673] VGAM551 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM551 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM551 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM551 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM551 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7674] The complementary binding of VGAM551 RNA, herein designated VGAM RNA, to host target binding sites on VGAM551 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM551 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM551 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7675] It is appreciated that VGAM551 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM551 host target genes. The mRNA of each one of this plurality of VGAM551 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM551 RNA, herein designated VGAM RNA, and which when bound by VGAM551 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM551 host target proteins.

[7676] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM551 gene, herein designated VGAM GENE, on one or more VGAM551 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7677] It is yet further appreciated that a function of VGAM551 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM551 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM551 correlate with, and may be deduced from, the identity of the host target genes which VGAM551 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7678] Nucleotide sequences of the VGAM551 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM551 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM551 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM551 are further described hereinbelow with reference to Table 1.

[7679] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM551 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7680] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 552 (VGAM552) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7681] VGAM552 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM552 was detected is described hereinabove with reference to Figs. 2-8.

[7682] VGAM552 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM552 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7683] VGAM552 gene, herein designated VGAM GENE, encodes a

VGAM552 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM552 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM552 precursor RNA is designated SEQ ID:14450, and is provided hereinbelow with reference to the sequence listing part.

[7684] VGAM552 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM552 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7685] An enzyme complex designated DICER COMPLEX, dices the VGAM552 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM552 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM552 RNA is designated SEQ ID:14451, and is provided hereinbelow with reference to the sequence listing part.

[7686] VGAM552 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM552 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM552 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7687] VGAM552 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM552 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM552 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed



sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM552 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM552 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7688] The complementary binding of VGAM552 RNA, herein designated VGAM RNA, to host target binding sites on VGAM552 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM552 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM552 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[7689] It is appreciated that VGAM552 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM552 host target genes. The mRNA of each one of this plurality of VGAM552 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM552 RNA, herein designated VGAM RNA, and which when bound by VGAM552 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM552 host target proteins.

[7690] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM552 gene, herein designated VGAM GENE, on one or more VGAM552 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7691] It is yet further appreciated that a function of VGAM552 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM552 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM552 correlate with, and may be deduced from, the identity of the host target genes which VGAM552 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7692] Nucleotide sequences of the VGAM552 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM552 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM552 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM552 are further described hereinbelow with reference to Table 1.

[7693] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM552 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7694] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 553 (VGAM553) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7695] VGAM553 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM553 was detected is described hereinabove with reference to Figs. 2-8.

[7696] VGAM553 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM553 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7697] VGAM553 gene, herein designated VGAM GENE, encodes a VGAM553 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM553 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM553 precursor RNA is designated SEQ ID:14464, and is provided hereinbelow with reference to the sequence listing part.

[7698] VGAM553 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM553 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7699] An enzyme complex designated DICER COMPLEX, dices the VGAM553 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM553 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM553 RNA is designated SEQ ID:14465, and is provided hereinbelow with reference to the sequence listing part.

[7700] VGAM553 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM553 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM553 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7701] VGAM553 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM553 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM553 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM553 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM553 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7702] The complementary binding of VGAM553 RNA, herein designated VGAM RNA, to host target binding sites on VGAM553 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM553 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM553 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7703] It is appreciated that VGAM553 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM553 host target genes. The mRNA of each one of this plurality of VGAM553 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM553 RNA, herein designated VGAM RNA, and which when bound by VGAM553 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM553 host target proteins.

[7704] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM553 gene, herein designated VGAM GENE, on one or more VGAM553 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-



though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7705] It is yet further appreciated that a function of VGAM553 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM553 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM553 correlate with, and may be deduced from, the identity of the host target genes which VGAM553 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7706] Nucleotide sequences of the VGAM553 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM553 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM553 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM553 are further described hereinbelow with reference to Table 1.

[7707] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM553 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7708] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 554 (VGAM554) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7709] VGAM554 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM554 was detected is described hereinabove with reference to Figs. 2–8.

[7710] VGAM554 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sesbania mosaic virus. VGAM554 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7711] VGAM554 gene, herein designated VGAM GENE, encodes a VGAM554 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM554 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM554 precursor RNA is designated SEQ ID:14497, and is provided hereinbelow with reference to the sequence listing part.

[7712] VGAM554 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM554 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7713] An enzyme complex designated DICER COMPLEX, dices the VGAM554 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM554 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM554 RNA is designated SEQ ID:14498, and is provided hereinbelow with reference to the sequence listing part.

[7714] VGAM554 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM554 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM554 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7715] VGAM554 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM554 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM554 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM554 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM554 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7716] The complementary binding of VGAM554 RNA, herein designated VGAM RNA, to host target binding sites on VGAM554 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM554 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM554 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7717] It is appreciated that VGAM554 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM554 host target genes. The mRNA of each one of this plurality of VGAM554 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM554 RNA, herein designated VGAM RNA, and which when bound by VGAM554 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM554 host target proteins.

[7718] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM554 gene, herein designated VGAM GENE, on one or more VGAM554 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7719] It is yet further appreciated that a function of VGAM554 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM554 include diagnosis, prevention and treatment of viral infection by Sesbania mosaic virus. Specific functions, and accordingly utilities, of VGAM554 correlate with, and may be deduced from, the identity of the host target genes which VGAM554 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7720] Nucleotide sequences of the VGAM554 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM554 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM554 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM554 are further described hereinbelow with reference to Table 1.

[7721] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM554 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7722] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 555 (VGAM555) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7723] VGAM555 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM555 was detected is described hereinabove with reference to Figs. 2–8.

[7724] VGAM555 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sesbania mosaic virus. VGAM555 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7725] VGAM555 gene, herein designated VGAM GENE, encodes a VGAM555 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM555 precursor RNA, herein



designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM555 precursor RNA is designated SEQ ID:14510, and is provided hereinbelow with reference to the sequence listing part.

[7726] VGAM555 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM555 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7727] An enzyme complex designated DICER COMPLEX, dices the VGAM555 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM555 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM555 RNA is designated SEQ ID:14511, and is provided hereinbelow with reference to the sequence listing part.

[7728] VGAM555 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM555 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM555 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7729] VGAM555 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM555 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM555 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM555 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM555 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7730] The complementary binding of VGAM555 RNA, herein designated VGAM RNA, to host target binding sites on VGAM555 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM555 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM555 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7731] It is appreciated that VGAM555 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM555 host target genes. The mRNA of each one of this plurality of VGAM555 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM555 RNA, herein designated VGAM RNA, and which when bound by VGAM555 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM555 host target proteins.

[7732] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM555 gene, herein designated VGAM GENE, on one or more VGAM555 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[7733] It is yet further appreciated that a function of VGAM555 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM555 include diagnosis, prevention and treatment of viral infection by Sesbania mosaic virus. Specific functions, and accordingly utilities, of VGAM555 correlate with, and may be deduced from, the identity of the host target genes which VGAM555 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7734] Nucleotide sequences of the VGAM555 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM555 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM555 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM555 are further described hereinbelow with reference to Table 1.

[7735] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM555 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7736] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 556 (VGAM556) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7737] VGAM556 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM556 was detected is described hereinabove with reference to Figs. 2–8.

[7738] VGAM556 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sesbania mosaic virus. VGAM556 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7739] VGAM556 gene, herein designated VGAM GENE, encodes a VGAM556 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM556 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM556 precursor RNA is designated SEQ ID:14527, and is provided hereinbelow with reference to the sequence listing part.

[7740] VGAM556 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM556 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7741] An enzyme complex designated DICER COMPLEX, dices the VGAM556 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM556 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM556 RNA is designated SEQ ID:14528, and is provided hereinbelow with reference to the sequence listing part.

[7742] VGAM556 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM556 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM556 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7743] VGAM556 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM556 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM556 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-



preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM556 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM556 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7744] The complementary binding of VGAM556 RNA, herein designated VGAM RNA, to host target binding sites on VGAM556 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM556 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM556 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7745] It is appreciated that VGAM556 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM556 host target genes. The mRNA of

each one of this plurality of VGAM556 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM556 RNA, herein designated VGAM RNA, and which when bound by VGAM556 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM556 host target proteins.

[7746] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM556 gene, herein designated VGAM GENE, on one or more VGAM556 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[7747] It is yet further appreciated that a function of VGAM556 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM556 include diagnosis, prevention and treatment of viral infection by Sesbania mosaic virus. Specific functions, and accordingly utilities, of VGAM556 correlate with, and may be deduced from, the identity of the host target genes which VGAM556 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7748] Nucleotide sequences of the VGAM556 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM556 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM556 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM556 are further described hereinbelow with reference to Table 1.

[7749] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM556 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[7750] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 557 (VGAM557) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7751] VGAM557 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM557 was detected is described hereinabove with reference to Figs. 2–8.

[7752] VGAM557 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM557 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7753] VGAM557 gene, herein designated VGAM GENE, encodes a VGAM557 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM557 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM557 precursor RNA is designated SEQ ID:14536, and is provided hereinbelow with reference to the sequence listing part.

[7754] VGAM557 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM557 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7755] An enzyme complex designated DICER COMPLEX, dices the VGAM557 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM557 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM557 RNA is designated SEQ ID:14537, and

is provided hereinbelow with reference to the sequence listing part.

[7756] VGAM557 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM557 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM557 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7757] VGAM557 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM557 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM557 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM557 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM557 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7758] The complementary binding of VGAM557 RNA, herein designated VGAM RNA, to host target binding sites on VGAM557 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM557 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM557 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7759] It is appreciated that VGAM557 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM557 host target genes. The mRNA of each one of this plurality of VGAM557 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM557 RNA, herein designated VGAM RNA, and which when bound by VGAM557 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM557 host target proteins.

[7760] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM557 gene, herein designated VGAM GENE, on one or more VGAM557 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).



[7761] It is yet further appreciated that a function of VGAM557 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM557 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM557 correlate with, and may be deduced from, the identity of the host target genes which VGAM557 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7762] Nucleotide sequences of the VGAM557 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM557 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM557 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM557 are further described hereinbelow with reference to Table 1.

[7763] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM557 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7764] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 558 (VGAM558) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7765] VGAM558 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM558 was detected is described hereinabove with reference to Figs. 2–8.

[7766] VGAM558 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM558 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7767] VGAM558 gene, herein designated VGAM GENE, encodes a VGAM558 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM558 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM558 precursor RNA is

designated SEQ ID:14572, and is provided hereinbelow with reference to the sequence listing part.

[7768] VGAM558 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM558 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7769] An enzyme complex designated DICER COMPLEX, dices the VGAM558 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM558 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM558 RNA is designated SEQ ID:14573, and is provided hereinbelow with reference to the sequence

listing part.

[7770] VGAM558 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM558 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM558 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7771] VGAM558 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM558 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM558 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM558 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM558 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7772] The complementary binding of VGAM558 RNA, herein designated VGAM RNA, to host target binding sites on VGAM558 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM558 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM558 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7773] It is appreciated that VGAM558 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM558 host target genes. The mRNA of each one of this plurality of VGAM558 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM558 RNA, herein designated VGAM RNA, and which when bound by VGAM558 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM558 host target proteins.

[7774] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM558 gene, herein designated VGAM GENE, on one or more VGAM558 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7775] It is yet further appreciated that a function of VGAM558 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM558 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM558 correlate with, and may be deduced from, the identity of the host target genes which VGAM558 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[7776] Nucleotide sequences of the VGAM558 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM558 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM558 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM558 are further described hereinbelow with reference to Table 1.

[7777] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM558 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7778] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 559 (VGAM559) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7779] VGAM559 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM559 was detected is described hereinabove with reference to Figs. 2–8.

[7780] VGAM559 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM559 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7781] VGAM559 gene, herein designated VGAM GENE, encodes a VGAM559 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM559 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM559 precursor RNA is designated SEQ ID:14576, and is provided hereinbelow



with reference to the sequence listing part.

[7782] VGAM559 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM559 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7783] An enzyme complex designated DICER COMPLEX, dices the VGAM559 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM559 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM559 RNA is designated SEQ ID:14577, and is provided hereinbelow with reference to the sequence listing part.

[7784] VGAM559 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM559 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM559 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7785] VGAM559 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM559 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM559 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM559 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM559 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7786] The complementary binding of VGAM559 RNA, herein designated VGAM RNA, to host target binding sites on VGAM559 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM559 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM559 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7787] It is appreciated that VGAM559 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM559 host target genes. The mRNA of each one of this plurality of VGAM559 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM559 RNA, herein designated VGAM RNA, and which when bound by VGAM559 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM559 host target proteins.

[7788] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM559 gene, herein designated VGAM GENE, on one or more VGAM559 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7789] It is yet further appreciated that a function of VGAM559 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM559 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM559 correlate with, and may be deduced from, the identity of the host target genes which VGAM559 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7790] Nucleotide sequences of the VGAM559 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM559 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM559 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM559 are further described hereinbelow with reference to Table 1.

[7791] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM559 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7792] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 560 (VGAM560) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7793] VGAM560 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM560 was detected is described hereinabove with reference to Figs. 2–8.

[7794] VGAM560 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM560 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7795] VGAM560 gene, herein designated VGAM GENE, encodes a VGAM560 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM560 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM560 precursor RNA is designated SEQ ID:14582, and is provided hereinbelow with reference to the sequence listing part.

[7796] VGAM560 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM560 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7797] An enzyme complex designated DICER COMPLEX, dices the VGAM560 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM560 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM560 RNA is designated SEQ ID:14583, and is provided hereinbelow with reference to the sequence listing part.

[7798] VGAM560 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM560 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM560 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7799] VGAM560 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM560 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM560 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM560 RNA, herein designated VGAM RNA, may have a different number of host target



binding sites in untranslated regions of a VGAM560 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7800] The complementary binding of VGAM560 RNA, herein designated VGAM RNA, to host target binding sites on VGAM560 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM560 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM560 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7801] It is appreciated that VGAM560 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM560 host target genes. The mRNA of each one of this plurality of VGAM560 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM560 RNA, herein designated VGAM

RNA, and which when bound by VGAM560 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM560 host target proteins.

[7802] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM560 gene, herein designated VGAM GENE, on one or more VGAM560 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7803] It is yet further appreciated that a function of VGAM560 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM560 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM560 correlate with, and may be deduced from, the identity of the host target genes which VGAM560 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7804] Nucleotide sequences of the VGAM560 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM560 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM560 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM560 are further described hereinbelow with reference to Table 1.

[7805] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM560 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7806] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 561 (VGAM561) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7807] VGAM561 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM561 was detected is described hereinabove with reference to Figs. 2–8.

[7808] VGAM561 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM561 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7809] VGAM561 gene, herein designated VGAM GENE, encodes a VGAM561 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM561 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM561 precursor RNA is designated SEQ ID:14604, and is provided hereinbelow with reference to the sequence listing part.

[7810] VGAM561 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM561 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7811] An enzyme complex designated DICER COMPLEX, dices the VGAM561 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM561 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM561 RNA is designated SEQ ID:14605, and is provided hereinbelow with reference to the sequence listing part.

[7812] VGAM561 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM561 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM561 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7813] VGAM561 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM561 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM561 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM561 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM561 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7814] The complementary binding of VGAM561 RNA, herein designated VGAM RNA, to host target binding sites on VGAM561 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM561 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM561 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7815] It is appreciated that VGAM561 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM561 host target genes. The mRNA of each one of this plurality of VGAM561 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM561 RNA, herein designated VGAM RNA, and which when bound by VGAM561 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM561 host target proteins.

[7816] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM561 gene, herein designated VGAM GENE, on one or more VGAM561 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7817] It is yet further appreciated that a function of VGAM561 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM561 include diagnosis, prevention and



treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM561 correlate with, and may be deduced from, the identity of the host target genes which VGAM561 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7818] Nucleotide sequences of the VGAM561 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM561 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM561 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM561 are further described hereinbelow with reference to Table 1.

[7819] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM561 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7820] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 562 (VGAM562) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7821] VGAM562 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM562 was detected is described hereinabove with reference to Figs. 2–8.

[7822] VGAM562 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM562 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7823] VGAM562 gene, herein designated VGAM GENE, encodes a VGAM562 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM562 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM562 precursor RNA is designated SEQ ID:14609, and is provided hereinbelow with reference to the sequence listing part.

[7824] VGAM562 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM562 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7825] An enzyme complex designated DICER COMPLEX, dices the VGAM562 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM562 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM562 RNA is designated SEQ ID:14610, and is provided hereinbelow with reference to the sequence listing part.

[7826] VGAM562 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM562 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM562 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7827] VGAM562 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM562 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM562 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM562 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM562 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7828] The complementary binding of VGAM562 RNA, herein designated VGAM RNA, to host target binding sites on VGAM562 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM562 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM562 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7829] It is appreciated that VGAM562 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM562 host target genes. The mRNA of each one of this plurality of VGAM562 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM562 RNA, herein designated VGAM RNA, and which when bound by VGAM562 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM562 host target proteins.

[7830] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM562 gene, herein designated VGAM GENE, on one or more VGAM562 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7831] It is yet further appreciated that a function of VGAM562 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM562 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1.

Specific functions, and accordingly utilities, of VGAM562 correlate with, and may be deduced from, the identity of the host target genes which VGAM562 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7832] Nucleotide sequences of the VGAM562 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM562 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM562 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM562 are further described hereinbelow with reference to Table 1.

[7833] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM562 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7834] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 563 (VGAM563) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[7835] VGAM563 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM563 was detected is described hereinabove with reference to Figs. 2–8.

[7836] VGAM563 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM563 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7837] VGAM563 gene, herein designated VGAM GENE, encodes a VGAM563 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM563 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM563 precursor RNA is designated SEQ ID:14652, and is provided hereinbelow with reference to the sequence listing part.

[7838] VGAM563 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM563 folded precursor RNA, herein designated VGAM FOLDED PRECUR-



SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7839] An enzyme complex designated DICER COMPLEX, dices the VGAM563 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM563 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM563 RNA is designated SEQ ID:14653, and is provided hereinbelow with reference to the sequence listing part.

[7840] VGAM563 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM563 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM563 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7841] VGAM563 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM563 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM563 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM563 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM563 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7842] The complementary binding of VGAM563 RNA, herein designated VGAM RNA, to host target binding sites on VGAM563 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM563 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM563 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7843] It is appreciated that VGAM563 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM563 host target genes. The mRNA of each one of this plurality of VGAM563 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM563 RNA, herein designated VGAM RNA, and which when bound by VGAM563 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM563 host target proteins.

[7844] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM563 gene, herein designated VGAM GENE, on one or more VGAM563 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7845] It is yet further appreciated that a function of VGAM563 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM563 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM563 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM563 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7846] Nucleotide sequences of the VGAM563 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM563 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM563 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM563 are further described hereinbelow with reference to Table 1.

[7847] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM563 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7848] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 564 (VGAM564) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[7849] VGAM564 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM564 was detected is described hereinabove with reference to Figs. 2–8.

[7850] VGAM564 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM564 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7851] VGAM564 gene, herein designated VGAM GENE, encodes a VGAM564 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM564 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM564 precursor RNA is designated SEQ ID:14680, and is provided hereinbelow with reference to the sequence listing part.

[7852] VGAM564 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM564 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7853] An enzyme complex designated DICER COMPLEX, dices the VGAM564 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM564 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM564 RNA is designated SEQ ID:14681, and is provided hereinbelow with reference to the sequence listing part.

[7854] VGAM564 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM564 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM564 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7855] VGAM564 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM564 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM564 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM564 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM564 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an



example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7856] The complementary binding of VGAM564 RNA, herein designated VGAM RNA, to host target binding sites on VGAM564 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM564 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM564 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7857] It is appreciated that VGAM564 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM564 host target genes. The mRNA of each one of this plurality of VGAM564 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM564 RNA, herein designated VGAM RNA, and which when bound by VGAM564 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM564 host target proteins.

[7858] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM564 gene, herein designated VGAM GENE, on one or more VGAM564 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7859] It is yet further appreciated that a function of VGAM564 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM564 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM564 correlate with, and may be deduced from, the identity of

the host target genes which VGAM564 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7860] Nucleotide sequences of the VGAM564 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM564 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM564 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM564 are further described hereinbelow with reference to Table 1.

[7861] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM564 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7862] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 565 (VGAM565) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7863] VGAM565 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM565 was detected is described hereinabove with reference to Figs. 2–8.

[7864] VGAM565 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM565 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7865] VGAM565 gene, herein designated VGAM GENE, encodes a VGAM565 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM565 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM565 precursor RNA is designated SEQ ID:14691, and is provided hereinbelow with reference to the sequence listing part.

[7866] VGAM565 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM565 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7867] An enzyme complex designated DICER COMPLEX, dices the VGAM565 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM565 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM565 RNA is designated SEQ ID:14692, and is provided hereinbelow with reference to the sequence listing part.

[7868] VGAM565 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM565 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM565 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7869] VGAM565 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM565 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM565 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM565 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM565 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7870] The complementary binding of VGAM565 RNA, herein designated VGAM RNA, to host target binding sites on VGAM565 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM565 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM565 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7871] It is appreciated that VGAM565 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM565 host target genes. The mRNA of each one of this plurality of VGAM565 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM565 RNA, herein designated VGAM RNA, and which when bound by VGAM565 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM565 host target proteins.

[7872] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM565 gene, herein designated VGAM GENE, on one or more VGAM565 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7873] It is yet further appreciated that a function of VGAM565 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM565 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM565 correlate with, and may be deduced from, the identity of the host target genes which VGAM565 binds and inhibits,



and the function of these host target genes, as elaborated hereinbelow.

[7874] Nucleotide sequences of the VGAM565 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM565 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM565 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM565 are further described hereinbelow with reference to Table 1.

[7875] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM565 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7876] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 566 (VGAM566) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7877] VGAM566 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM566 was detected is described hereinabove with reference to Figs. 2–8.

[7878] VGAM566 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM566 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7879] VGAM566 gene, herein designated VGAM GENE, encodes a VGAM566 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM566 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM566 precursor RNA is designated SEQ ID:14706, and is provided hereinbelow with reference to the sequence listing part.

[7880] VGAM566 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM566 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7881] An enzyme complex designated DICER COMPLEX, dices the VGAM566 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM566 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM566 RNA is designated SEQ ID:14707, and is provided hereinbelow with reference to the sequence listing part.

[7882] VGAM566 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM566 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM566 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7883] VGAM566 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM566 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM566 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM566 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM566 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[7884] The complementary binding of VGAM566 RNA, herein designated VGAM RNA, to host target binding sites on VGAM566 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM566 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM566 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7885] It is appreciated that VGAM566 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM566 host target genes. The mRNA of each one of this plurality of VGAM566 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM566 RNA, herein designated VGAM RNA, and which when bound by VGAM566 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM566 host target proteins.

[7886] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM566 gene, herein designated VGAM GENE, on one or more VGAM566 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7887] It is yet further appreciated that a function of VGAM566 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM566 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM566 correlate with, and may be deduced from, the identity of the host target genes which VGAM566 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[7888] Nucleotide sequences of the VGAM566 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM566 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM566 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM566 are further described hereinbelow with reference to Table 1.

[7889] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM566 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7890] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 567 (VGAM567) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7891] VGAM567 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM567 was detected is described hereinabove with reference to Figs. 2–8.

[7892] VGAM567 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM567 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7893] VGAM567 gene, herein designated VGAM GENE, encodes a VGAM567 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM567 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM567 precursor RNA is designated SEQ ID:14912, and is provided hereinbelow with reference to the sequence listing part.

[7894] VGAM567 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM567 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the



RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7895] An enzyme complex designated DICER COMPLEX, dices the VGAM567 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM567 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM567 RNA is designated SEQ ID:14913, and is provided hereinbelow with reference to the sequence listing part.

[7896] VGAM567 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM567 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM567 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[7897] VGAM567 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM567 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM567 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM567 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM567 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7898] The complementary binding of VGAM567 RNA, herein designated VGAM RNA, to host target binding sites on VGAM567 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM567 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM567 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7899] It is appreciated that VGAM567 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM567 host target genes. The mRNA of each one of this plurality of VGAM567 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM567 RNA, herein designated VGAM RNA, and which when bound by VGAM567 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM567 host target proteins.

[7900] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM567 gene, herein designated VGAM GENE, on one or

more VGAM567 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7901] It is yet further appreciated that a function of VGAM567 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM567 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM567 correlate with, and may be deduced from, the identity of the host target genes which VGAM567 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7902] Nucleotide sequences of the VGAM567 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM567 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM567 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM567 are further described hereinbelow with reference to Table 1.

[7903] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM567 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7904] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 568 (VGAM568) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7905] VGAM568 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM568 was detected is described

hereinabove with reference to Figs. 2–8.

[7906] VGAM568 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM568 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7907] VGAM568 gene, herein designated VGAM GENE, encodes a VGAM568 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM568 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM568 precursor RNA is designated SEQ ID:14940, and is provided hereinbelow with reference to the sequence listing part.

[7908] VGAM568 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM568 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7909] An enzyme complex designated DICER COMPLEX, dices the VGAM568 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM568 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM568 RNA is designated SEQ ID:14941, and is provided hereinbelow with reference to the sequence listing part.

[7910] VGAM568 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM568 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM568 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7911] VGAM568 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM568 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM568 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM568 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM568 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7912] The complementary binding of VGAM568 RNA, herein



designated VGAM RNA, to host target binding sites on VGAM568 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM568 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM568 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7913] It is appreciated that VGAM568 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM568 host target genes. The mRNA of each one of this plurality of VGAM568 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM568 RNA, herein designated VGAM RNA, and which when bound by VGAM568 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM568 host target proteins.

[7914] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM568 gene, herein designated VGAM GENE, on one or more VGAM568 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7915] It is yet further appreciated that a function of VGAM568 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM568 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM568 correlate with, and may be deduced from, the identity of the host target genes which VGAM568 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7916] Nucleotide sequences of the VGAM568 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM568 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM568 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM568 are further described hereinbelow with reference to Table 1.

[7917] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM568 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7918] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 569 (VGAM569) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7919] VGAM569 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM569 was detected is described hereinabove with reference to Figs. 2-8.

[7920] VGAM569 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM569 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7921] VGAM569 gene, herein designated VGAM GENE, encodes a VGAM569 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM569 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM569 precursor RNA is designated SEQ ID:14951, and is provided hereinbelow with reference to the sequence listing part.

[7922] VGAM569 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM569 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[7923] An enzyme complex designated DICER COMPLEX, dices the VGAM569 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM569 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM569 RNA is designated SEQ ID:14952, and is provided hereinbelow with reference to the sequence listing part.

[7924] VGAM569 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM569 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM569 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7925] VGAM569 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM569 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM569 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM569 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM569 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7926] The complementary binding of VGAM569 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM569 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM569 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM569 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7927] It is appreciated that VGAM569 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM569 host target genes. The mRNA of each one of this plurality of VGAM569 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM569 RNA, herein designated VGAM RNA, and which when bound by VGAM569 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM569 host target proteins.

[7928] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM569 gene, herein designated VGAM GENE, on one or more VGAM569 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7929] It is yet further appreciated that a function of VGAM569 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM569 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM569 correlate with, and may be deduced from, the identity of the host target genes which VGAM569 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7930] Nucleotide sequences of the VGAM569 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



diced VGAM569 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM569 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM569 are further described hereinbelow with reference to Table 1.

[7931] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM569 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7932] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 570 (VGAM570) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7933] VGAM570 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM570 was detected is described hereinabove with reference to Figs. 2-8.

[7934] VGAM570 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Saimiriine herpesvirus 2. VGAM570 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7935] VGAM570 gene, herein designated VGAM GENE, encodes a VGAM570 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM570 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM570 precursor RNA is designated SEQ ID:14958, and is provided hereinbelow with reference to the sequence listing part.

[7936] VGAM570 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM570 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7937] An enzyme complex designated DICER COMPLEX, dices the VGAM570 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM570 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM570 RNA is designated SEQ ID:14959, and is provided hereinbelow with reference to the sequence listing part.

[7938] VGAM570 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM570 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM570 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7939] VGAM570 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM570 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM570 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM570 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM570 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7940] The complementary binding of VGAM570 RNA, herein designated VGAM RNA, to host target binding sites on VGAM570 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM570 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM570 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7941] It is appreciated that VGAM570 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM570 host target genes. The mRNA of each one of this plurality of VGAM570 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM570 RNA, herein designated VGAM RNA, and which when bound by VGAM570 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM570 host target proteins.

[7942] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM570 gene, herein designated VGAM GENE, on one or more VGAM570 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7943] It is yet further appreciated that a function of VGAM570 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM570 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM570 correlate with, and may be deduced from, the identity of the host target genes which VGAM570 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7944] Nucleotide sequences of the VGAM570 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM570 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM570 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM570 are further described hereinbelow with reference to Table 1.

[7945] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM570 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7946] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 571 (VGAM571) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7947] VGAM571 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM571 was detected is described hereinabove with reference to Figs. 2-8.

[7948] VGAM571 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2.

VGAM571 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7949] VGAM571 gene, herein designated VGAM GENE, encodes a VGAM571 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM571 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM571 precursor RNA is designated SEQ ID:15010, and is provided hereinbelow with reference to the sequence listing part.

[7950] VGAM571 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM571 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7951] An enzyme complex designated DICER COMPLEX, dices



the VGAM571 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM571 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM571 RNA is designated SEQ ID:15011, and is provided hereinbelow with reference to the sequence listing part.

[7952] VGAM571 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM571 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM571 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7953] VGAM571 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM571 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM571 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM571 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM571 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7954] The complementary binding of VGAM571 RNA, herein designated VGAM RNA, to host target binding sites on VGAM571 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM571 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM571 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7955] It is appreciated that VGAM571 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM571 host target genes. The mRNA of each one of this plurality of VGAM571 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM571 RNA, herein designated VGAM RNA, and which when bound by VGAM571 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM571 host target proteins.

[7956] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM571 gene, herein designated VGAM GENE, on one or more VGAM571 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7957] It is yet further appreciated that a function of VGAM571 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM571 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM571 correlate with, and may be deduced from, the identity of the host target genes which VGAM571 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7958] Nucleotide sequences of the VGAM571 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM571 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM571 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM571 are further described hereinbelow with reference to Table 1.

[7959] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM571 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7960] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 572 (VGAM572) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7961] VGAM572 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM572 was detected is described hereinabove with reference to Figs. 2-8.

[7962] VGAM572 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV-2. VGAM572 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[7963] VGAM572 gene, herein designated VGAM GENE, encodes a VGAM572 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM572 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM572 precursor RNA is designated SEQ ID:15020, and is provided hereinbelow with reference to the sequence listing part.

[7964] VGAM572 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM572 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7965] An enzyme complex designated DICER COMPLEX, dices the VGAM572 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM572 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM572 RNA is designated SEQ ID:15021, and is provided hereinbelow with reference to the sequence listing part.

[7966] VGAM572 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM572 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM572 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7967] VGAM572 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM572 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM572 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM572 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM572 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7968] The complementary binding of VGAM572 RNA, herein designated VGAM RNA, to host target binding sites on VGAM572 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM572 host tar-



get RNA, herein designated VGAM HOST TARGET RNA, into VGAM572 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7969] It is appreciated that VGAM572 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM572 host target genes. The mRNA of each one of this plurality of VGAM572 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM572 RNA, herein designated VGAM RNA, and which when bound by VGAM572 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM572 host target proteins.

[7970] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM572 gene, herein designated VGAM GENE, on one or more VGAM572 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7971] It is yet further appreciated that a function of VGAM572 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM572 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-2. Specific functions, and accordingly utilities, of VGAM572 correlate with, and may be deduced from, the identity of the host target genes which VGAM572 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7972] Nucleotide sequences of the VGAM572 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM572 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM572 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM572 are further described hereinbelow with reference to Table 1.

[7973] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM572 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7974] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 573 (VGAM573) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7975] VGAM573 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM573 was detected is described hereinabove with reference to Figs. 2-8.

[7976] VGAM573 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV-2. VGAM573 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[7977] VGAM573 gene, herein designated VGAM GENE, encodes a VGAM573 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM573 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM573 precursor RNA is designated SEQ ID:15043, and is provided hereinbelow with reference to the sequence listing part.

[7978] VGAM573 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM573 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7979] An enzyme complex designated DICER COMPLEX, dices the VGAM573 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM573 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM573 RNA is designated SEQ ID:15044, and is provided hereinbelow with reference to the sequence listing part.

[7980] VGAM573 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM573 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM573 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7981] VGAM573 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM573 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM573 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM573 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM573 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7982] The complementary binding of VGAM573 RNA, herein designated VGAM RNA, to host target binding sites on VGAM573 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM573 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM573 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7983] It is appreciated that VGAM573 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM573 host target genes. The mRNA of each one of this plurality of VGAM573 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM573 RNA, herein designated VGAM RNA, and which when bound by VGAM573 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM573 host target proteins.

[7984] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM573 gene, herein designated VGAM GENE, on one or more VGAM573 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7985] It is yet further appreciated that a function of VGAM573 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM573 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-2. Specific functions, and accordingly utilities, of VGAM573 correlate with, and may be deduced from, the identity of the host target genes which VGAM573 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7986] Nucleotide sequences of the VGAM573 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM573 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM573 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM573 are further de-



scribed hereinbelow with reference to Table 1.

[7987] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM573 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7988] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 574 (VGAM574) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7989] VGAM574 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM574 was detected is described hereinabove with reference to Figs. 2-8.

[7990] VGAM574 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM574 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7991] VGAM574 gene, herein designated VGAM GENE, encodes a VGAM574 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM574 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM574 precursor RNA is designated SEQ ID:15059, and is provided hereinbelow with reference to the sequence listing part.

[7992] VGAM574 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM574 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7993] An enzyme complex designated DICER COMPLEX, dices the VGAM574 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM574 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM574 RNA is designated SEQ ID:15060, and is provided hereinbelow with reference to the sequence listing part.

[7994] VGAM574 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM574 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM574 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[7995] VGAM574 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM574 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM574 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM574 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM574 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[7996] The complementary binding of VGAM574 RNA, herein designated VGAM RNA, to host target binding sites on VGAM574 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM574 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM574 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7997] It is appreciated that VGAM574 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM574 host target genes. The mRNA of each one of this plurality of VGAM574 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM574 RNA, herein designated VGAM RNA, and which when bound by VGAM574 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM574 host target proteins.

[7998] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM574 gene, herein designated VGAM GENE, on one or more VGAM574 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[7999] It is yet further appreciated that a function of VGAM574 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM574 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM574 correlate with, and may be deduced from, the identity of the host target genes which VGAM574 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8000] Nucleotide sequences of the VGAM574 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM574 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM574 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM574 are further described hereinbelow with reference to Table 1.

[8001] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM574 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8002] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 575 (VGAM575) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8003] VGAM575 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM575 was detected is described hereinabove with reference to Figs. 2-8.

[8004] VGAM575 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV-2. VGAM575 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8005] VGAM575 gene, herein designated VGAM GENE, encodes a

VGAM575 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM575 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM575 precursor RNA is designated SEQ ID:15123, and is provided hereinbelow with reference to the sequence listing part.

[8006] VGAM575 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM575 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8007] An enzyme complex designated DICER COMPLEX, dices the VGAM575 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM575 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM575 RNA is designated SEQ ID:15124, and is provided hereinbelow with reference to the sequence listing part.

[8008] VGAM575 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM575 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM575 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8009] VGAM575 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM575 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM575 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM575 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM575 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8010] The complementary binding of VGAM575 RNA, herein designated VGAM RNA, to host target binding sites on VGAM575 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM575 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM575 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[8011] It is appreciated that VGAM575 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM575 host target genes. The mRNA of each one of this plurality of VGAM575 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM575 RNA, herein designated VGAM RNA, and which when bound by VGAM575 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM575 host target proteins.

[8012] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM575 gene, herein designated VGAM GENE, on one or more VGAM575 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8013] It is yet further appreciated that a function of VGAM575 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM575 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-2. Specific functions, and accordingly utilities, of VGAM575 correlate with, and may be deduced from, the identity of the host target genes which VGAM575 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8014] Nucleotide sequences of the VGAM575 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM575 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM575 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM575 are further described hereinbelow with reference to Table 1.

[8015] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM575 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8016] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 576 (VGAM576) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8017] VGAM576 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM576 was detected is described hereinabove with reference to Figs. 2-8.

[8018] VGAM576 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM576 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8019] VGAM576 gene, herein designated VGAM GENE, encodes a VGAM576 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM576 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM576 precursor RNA is designated SEQ ID:15143, and is provided hereinbelow with reference to the sequence listing part.

[8020] VGAM576 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM576 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8021] An enzyme complex designated DICER COMPLEX, dices the VGAM576 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM576 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM576 RNA is designated SEQ ID:15144, and is provided hereinbelow with reference to the sequence listing part.

[8022] VGAM576 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM576 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM576 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8023] VGAM576 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM576 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM576 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM576 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM576 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8024] The complementary binding of VGAM576 RNA, herein designated VGAM RNA, to host target binding sites on VGAM576 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM576 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM576 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[8025] It is appreciated that VGAM576 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM576 host target genes. The mRNA of each one of this plurality of VGAM576 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM576 RNA, herein designated VGAM RNA, and which when bound by VGAM576 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM576 host target proteins.

[8026] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM576 gene, herein designated VGAM GENE, on one or more VGAM576 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8027] It is yet further appreciated that a function of VGAM576 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM576 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM576 correlate with, and may be deduced from, the identity of the host target genes which VGAM576 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8028] Nucleotide sequences of the VGAM576 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM576 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM576 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM576 are further described hereinbelow with reference to Table 1.

[8029] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM576 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8030] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 577 (VGAM577) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8031] VGAM577 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM577 was detected is described hereinabove with reference to Figs. 2–8.

[8032] VGAM577 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey adenovirus 3. VGAM577 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8033] VGAM577 gene, herein designated VGAM GENE, encodes a VGAM577 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM577 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM577 precursor RNA is designated SEQ ID:15232, and is provided hereinbelow with reference to the sequence listing part.

[8034] VGAM577 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM577 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8035] An enzyme complex designated DICER COMPLEX, dices the VGAM577 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM577 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM577 RNA is designated SEQ ID:15233, and is provided hereinbelow with reference to the sequence listing part.

[8036] VGAM577 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM577 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM577 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8037] VGAM577 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM577 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM577 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM577 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM577 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8038] The complementary binding of VGAM577 RNA, herein designated VGAM RNA, to host target binding sites on VGAM577 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM577 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM577 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8039] It is appreciated that VGAM577 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM577 host target genes. The mRNA of each one of this plurality of VGAM577 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM577 RNA, herein designated VGAM RNA, and which when bound by VGAM577 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM577 host target proteins.

[8040] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM577 gene, herein designated VGAM GENE, on one or more VGAM577 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8041] It is yet further appreciated that a function of VGAM577 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM577 include diagnosis, prevention and treatment of viral infection by Turkey adenovirus 3. Specific functions, and accordingly utilities, of VGAM577 correlate with, and may be deduced from, the identity of the host target genes which VGAM577 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8042] Nucleotide sequences of the VGAM577 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM577 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM577 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM577 are further described hereinbelow with reference to Table 1.

[8043] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the



complementarity of each of these host target binding sites to VGAM577 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8044] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 578 (VGAM578) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8045] VGAM578 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM578 was detected is described hereinabove with reference to Figs. 2–8.

[8046] VGAM578 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey adenovirus 3. VGAM578 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8047] VGAM578 gene, herein designated VGAM GENE, encodes a VGAM578 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM578 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM578 precursor RNA is designated SEQ ID:15241, and is provided hereinbelow with reference to the sequence listing part.

[8048] VGAM578 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM578 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8049] An enzyme complex designated DICER COMPLEX, dices the VGAM578 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM578 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM578 RNA is designated SEQ ID:15242, and is provided hereinbelow with reference to the sequence listing part.

[8050] VGAM578 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM578 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM578 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8051] VGAM578 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM578 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM578 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM578 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM578 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8052] The complementary binding of VGAM578 RNA, herein designated VGAM RNA, to host target binding sites on VGAM578 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM578 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM578 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8053] It is appreciated that VGAM578 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM578 host target genes. The mRNA of each one of this plurality of VGAM578 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM578 RNA, herein designated VGAM RNA, and which when bound by VGAM578 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM578 host target proteins.

[8054] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM578 gene, herein designated VGAM GENE, on one or more VGAM578 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[8055] It is yet further appreciated that a function of VGAM578 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM578 include diagnosis, prevention and treatment of viral infection by Turkey adenovirus 3. Specific functions, and accordingly utilities, of VGAM578 correlate with, and may be deduced from, the identity of the host target genes which VGAM578 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8056] Nucleotide sequences of the VGAM578 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM578 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM578 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM578 are further described hereinbelow with reference to Table 1.

[8057] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM578 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8058] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 579 (VGAM579) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8059] VGAM579 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM579 was detected is described hereinabove with reference to Figs. 2–8.

[8060] VGAM579 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey adenovirus 3. VGAM579 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8061] VGAM579 gene, herein designated VGAM GENE, encodes a VGAM579 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM579 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM579 precursor RNA is designated SEQ ID:15246, and is provided hereinbelow with reference to the sequence listing part.

[8062] VGAM579 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM579 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8063] An enzyme complex designated DICER COMPLEX, dices the VGAM579 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM579 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-



quence of VGAM579 RNA is designated SEQ ID:15247, and is provided hereinbelow with reference to the sequence listing part.

[8064] VGAM579 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM579 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM579 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8065] VGAM579 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM579 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM579 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM579 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM579 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8066] The complementary binding of VGAM579 RNA, herein designated VGAM RNA, to host target binding sites on VGAM579 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM579 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM579 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8067] It is appreciated that VGAM579 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM579 host target genes. The mRNA of

each one of this plurality of VGAM579 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM579 RNA, herein designated VGAM RNA, and which when bound by VGAM579 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM579 host target proteins.

[8068] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM579 gene, herein designated VGAM GENE, on one or more VGAM579 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[8069] It is yet further appreciated that a function of VGAM579 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM579 include diagnosis, prevention and treatment of viral infection by Turkey adenovirus 3. Specific functions, and accordingly utilities, of VGAM579 correlate with, and may be deduced from, the identity of the host target genes which VGAM579 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8070] Nucleotide sequences of the VGAM579 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM579 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM579 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM579 are further described hereinbelow with reference to Table 1.

[8071] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM579 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[8072] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 580 (VGAM580) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8073] VGAM580 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM580 was detected is described hereinabove with reference to Figs. 2–8.

[8074] VGAM580 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey adenovirus 3. VGAM580 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8075] VGAM580 gene, herein designated VGAM GENE, encodes a VGAM580 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM580 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM580 precursor RNA is designated SEQ ID:15261, and is provided hereinbelow with reference to the sequence listing part.

[8076] VGAM580 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM580 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8077] An enzyme complex designated DICER COMPLEX, dices the VGAM580 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM580 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM580 RNA is designated SEQ ID:15262, and

is provided hereinbelow with reference to the sequence listing part.

[8078] VGAM580 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM580 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM580 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8079] VGAM580 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM580 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM580 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM580 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM580 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8080] The complementary binding of VGAM580 RNA, herein designated VGAM RNA, to host target binding sites on VGAM580 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM580 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM580 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8081] It is appreciated that VGAM580 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM580 host target genes. The mRNA of each one of this plurality of VGAM580 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM580 RNA, herein designated VGAM RNA, and which when bound by VGAM580 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM580 host target proteins.

[8082] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM580 gene, herein designated VGAM GENE, on one or more VGAM580 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8083] It is yet further appreciated that a function of VGAM580 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM580 include diagnosis, prevention and treatment of viral infection by Turkey adenovirus 3. Specific functions, and accordingly utilities, of VGAM580 correlate with, and may be deduced from, the identity of the host target genes which VGAM580 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8084] Nucleotide sequences of the VGAM580 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM580 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM580 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM580 are further described hereinbelow with reference to Table 1.

[8085] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM580 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8086] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 581 (VGAM581) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8087] VGAM581 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM581 was detected is described hereinabove with reference to Figs. 2–8.

[8088] VGAM581 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM581 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8089] VGAM581 gene, herein designated VGAM GENE, encodes a VGAM581 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM581 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM581 precursor RNA is

designated SEQ ID:15273, and is provided hereinbelow with reference to the sequence listing part.

[8090] VGAM581 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM581 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8091] An enzyme complex designated DICER COMPLEX, dices the VGAM581 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM581 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM581 RNA is designated SEQ ID:15274, and is provided hereinbelow with reference to the sequence

listing part.

[8092] VGAM581 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM581 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM581 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8093] VGAM581 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM581 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM581 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM581 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM581 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8094] The complementary binding of VGAM581 RNA, herein designated VGAM RNA, to host target binding sites on VGAM581 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM581 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM581 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8095] It is appreciated that VGAM581 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM581 host target genes. The mRNA of each one of this plurality of VGAM581 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM581 RNA, herein designated VGAM RNA, and which when bound by VGAM581 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM581 host target proteins.

[8096] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM581 gene, herein designated VGAM GENE, on one or more VGAM581 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8097] It is yet further appreciated that a function of VGAM581 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM581 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM581 correlate with, and may be deduced from, the identity of the host target genes which VGAM581 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8098] Nucleotide sequences of the VGAM581 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM581 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM581 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM581 are further described hereinbelow with reference to Table 1.

[8099] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM581 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8100] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 582 (VGAM582) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8101] VGAM582 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM582 was detected is described hereinabove with reference to Figs. 2–8.

[8102] VGAM582 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM582 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8103] VGAM582 gene, herein designated VGAM GENE, encodes a VGAM582 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM582 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM582 precursor RNA is designated SEQ ID:15287, and is provided hereinbelow

with reference to the sequence listing part.

[8104] VGAM582 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM582 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8105] An enzyme complex designated DICER COMPLEX, dices the VGAM582 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM582 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM582 RNA is designated SEQ ID:15288, and is provided hereinbelow with reference to the sequence listing part.

[8106] VGAM582 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM582 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM582 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8107] VGAM582 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM582 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM582 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM582 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM582 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8108] The complementary binding of VGAM582 RNA, herein designated VGAM RNA, to host target binding sites on VGAM582 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM582 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM582 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8109] It is appreciated that VGAM582 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM582 host target genes. The mRNA of each one of this plurality of VGAM582 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM582 RNA, herein designated VGAM RNA, and which when bound by VGAM582 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM582 host target proteins.

[8110] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM582 gene, herein designated VGAM GENE, on one or more VGAM582 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8111] It is yet further appreciated that a function of VGAM582 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM582 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM582 correlate with, and may be deduced from, the identity of the host target genes which VGAM582 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8112] Nucleotide sequences of the VGAM582 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM582 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM582 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM582 are further described hereinbelow with reference to Table 1.

[8113] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM582 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8114] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 583 (VGAM583) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8115] VGAM583 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM583 was detected is described hereinabove with reference to Figs. 2–8.

[8116] VGAM583 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM583 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8117] VGAM583 gene, herein designated VGAM GENE, encodes a VGAM583 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM583 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM583 precursor RNA is designated SEQ ID:15291, and is provided hereinbelow with reference to the sequence listing part.

[8118] VGAM583 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM583 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8119] An enzyme complex designated DICER COMPLEX, dices the VGAM583 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM583 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM583 RNA is designated SEQ ID:15292, and is provided hereinbelow with reference to the sequence listing part.

[8120] VGAM583 host target gene, herein designated VGAM



HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM583 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM583 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8121] VGAM583 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM583 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM583 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM583 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM583 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8122] The complementary binding of VGAM583 RNA, herein designated VGAM RNA, to host target binding sites on VGAM583 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM583 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM583 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8123] It is appreciated that VGAM583 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM583 host target genes. The mRNA of each one of this plurality of VGAM583 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM583 RNA, herein designated VGAM

RNA, and which when bound by VGAM583 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM583 host target proteins.

[8124] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM583 gene, herein designated VGAM GENE, on one or more VGAM583 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8125] It is yet further appreciated that a function of VGAM583 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM583 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM583 correlate with, and may be deduced from, the identity of the host target genes which VGAM583 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8126] Nucleotide sequences of the VGAM583 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM583 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM583 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM583 are further described hereinbelow with reference to Table 1.

[8127] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM583 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8128] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 584 (VGAM584) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8129] VGAM584 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM584 was detected is described hereinabove with reference to Figs. 2–8.

[8130] VGAM584 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM584 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8131] VGAM584 gene, herein designated VGAM GENE, encodes a VGAM584 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM584 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM584 precursor RNA is designated SEQ ID:15297, and is provided hereinbelow with reference to the sequence listing part.

[8132] VGAM584 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM584 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8133] An enzyme complex designated DICER COMPLEX, dices the VGAM584 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM584 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM584 RNA is designated SEQ ID:15298, and is provided hereinbelow with reference to the sequence listing part.

[8134] VGAM584 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM584 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM584 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8135] VGAM584 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM584 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM584 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM584 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM584 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8136] The complementary binding of VGAM584 RNA, herein designated VGAM RNA, to host target binding sites on VGAM584 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM584 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM584 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8137] It is appreciated that VGAM584 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM584 host target genes. The mRNA of each one of this plurality of VGAM584 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM584 RNA, herein designated VGAM RNA, and which when bound by VGAM584 RNA, herein



designated VGAM RNA, causes inhibition of translation of respective one or more VGAM584 host target proteins.

[8138] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM584 gene, herein designated VGAM GENE, on one or more VGAM584 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8139] It is yet further appreciated that a function of VGAM584 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM584 include diagnosis, prevention and

treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM584 correlate with, and may be deduced from, the identity of the host target genes which VGAM584 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8140] Nucleotide sequences of the VGAM584 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM584 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM584 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM584 are further described hereinbelow with reference to Table 1.

[8141] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM584 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8142] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 585 (VGAM585) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8143] VGAM585 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM585 was detected is described hereinabove with reference to Figs. 2–8.

[8144] VGAM585 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM585 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8145] VGAM585 gene, herein designated VGAM GENE, encodes a VGAM585 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM585 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM585 precursor RNA is designated SEQ ID:15309, and is provided hereinbelow with reference to the sequence listing part.

[8146] VGAM585 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM585 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8147] An enzyme complex designated DICER COMPLEX, dices the VGAM585 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM585 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM585 RNA is designated SEQ ID:15310, and is provided hereinbelow with reference to the sequence listing part.

[8148] VGAM585 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM585 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM585 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8149] VGAM585 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM585 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM585 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM585 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM585 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8150] The complementary binding of VGAM585 RNA, herein designated VGAM RNA, to host target binding sites on VGAM585 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM585 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM585 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8151] It is appreciated that VGAM585 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM585 host target genes. The mRNA of each one of this plurality of VGAM585 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM585 RNA, herein designated VGAM RNA, and which when bound by VGAM585 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM585 host target proteins.

[8152] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM585 gene, herein designated VGAM GENE, on one or more VGAM585 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8153] It is yet further appreciated that a function of VGAM585 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM585 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Spe-

cific functions, and accordingly utilities, of VGAM585 correlate with, and may be deduced from, the identity of the host target genes which VGAM585 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8154] Nucleotide sequences of the VGAM585 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM585 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM585 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM585 are further described hereinbelow with reference to Table 1.

[8155] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM585 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8156] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 586 (VGAM586) viral gene, which modulates expression of respective host target genes thereof, the func-



tion and utility of which host target genes is known in the art.

[8157] VGAM586 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM586 was detected is described hereinabove with reference to Figs. 2–8.

[8158] VGAM586 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM586 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8159] VGAM586 gene, herein designated VGAM GENE, encodes a VGAM586 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM586 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM586 precursor RNA is designated SEQ ID:15316, and is provided hereinbelow with reference to the sequence listing part.

[8160] VGAM586 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM586 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8161] An enzyme complex designated DICER COMPLEX, dices the VGAM586 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM586 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM586 RNA is designated SEQ ID:15317, and is provided hereinbelow with reference to the sequence listing part.

[8162] VGAM586 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM586 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM586 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8163] VGAM586 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM586 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM586 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM586 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM586 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8164] The complementary binding of VGAM586 RNA, herein designated VGAM RNA, to host target binding sites on VGAM586 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM586 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM586 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8165] It is appreciated that VGAM586 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM586 host target genes. The mRNA of each one of this plurality of VGAM586 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM586 RNA, herein designated VGAM RNA, and which when bound by VGAM586 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM586 host target proteins.

[8166] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM586 gene, herein designated VGAM GENE, on one or more VGAM586 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8167] It is yet further appreciated that a function of VGAM586 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM586 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM586 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM586 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8168] Nucleotide sequences of the VGAM586 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM586 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM586 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM586 are further described hereinbelow with reference to Table 1.

[8169] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM586 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8170] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 587 (VGAM587) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[8171] VGAM587 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM587 was detected is described hereinabove with reference to Figs. 2–8.

[8172] VGAM587 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A. VGAM587 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8173] VGAM587 gene, herein designated VGAM GENE, encodes a VGAM587 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM587 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM587 precursor RNA is designated SEQ ID:15326, and is provided hereinbelow with reference to the sequence listing part.

[8174] VGAM587 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM587 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8175] An enzyme complex designated DICER COMPLEX, dices the VGAM587 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM587 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM587 RNA is designated SEQ ID:15327, and is provided hereinbelow with reference to the sequence listing part.

[8176] VGAM587 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM587 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM587 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8177] VGAM587 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM587 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM587 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM587 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM587 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8178] The complementary binding of VGAM587 RNA, herein designated VGAM RNA, to host target binding sites on VGAM587 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM587 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM587 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8179] It is appreciated that VGAM587 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM587 host target genes. The mRNA of each one of this plurality of VGAM587 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM587 RNA, herein designated VGAM RNA, and which when bound by VGAM587 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM587 host target proteins.

[8180] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM587 gene, herein designated VGAM GENE, on one or more VGAM587 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8181] It is yet further appreciated that a function of VGAM587 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM587 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM587 correlate with, and may be deduced from, the identity of the host target genes which VGAM587 binds and inhibits, and the

function of these host target genes, as elaborated herein—below.

[8182] Nucleotide sequences of the VGAM587 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM587 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM587 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM587 are further described hereinbelow with reference to Table 1.

[8183] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM587 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8184] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 588 (VGAM588) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8185] VGAM588 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM588 was detected is described hereinabove with reference to Figs. 2–8.

[8186] VGAM588 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM588 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8187] VGAM588 gene, herein designated VGAM GENE, encodes a VGAM588 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM588 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM588 precursor RNA is designated SEQ ID:15333, and is provided hereinbelow with reference to the sequence listing part.

[8188] VGAM588 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM588 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8189] An enzyme complex designated DICER COMPLEX, dices the VGAM588 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM588 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM588 RNA is designated SEQ ID:15334, and is provided hereinbelow with reference to the sequence listing part.

[8190] VGAM588 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM588 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM588 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8191] VGAM588 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM588 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM588 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM588 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM588 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[8192] The complementary binding of VGAM588 RNA, herein designated VGAM RNA, to host target binding sites on VGAM588 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM588 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM588 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8193] It is appreciated that VGAM588 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM588 host target genes. The mRNA of each one of this plurality of VGAM588 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM588 RNA, herein designated VGAM RNA, and which when bound by VGAM588 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM588 host target proteins.

[8194] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM588 gene, herein designated VGAM GENE, on one or more VGAM588 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8195] It is yet further appreciated that a function of VGAM588 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM588 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM588 correlate with, and may be deduced from, the identity of the host target genes which VGAM588 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[8196] Nucleotide sequences of the VGAM588 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM588 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM588 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM588 are further described hereinbelow with reference to Table 1.

[8197] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM588 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8198] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 589 (VGAM589) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8199] VGAM589 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM589 was detected is described hereinabove with reference to Figs. 2–8.

[8200] VGAM589 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A.

VGAM589 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8201] VGAM589 gene, herein designated VGAM GENE, encodes a VGAM589 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM589 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM589 precursor RNA is designated SEQ ID:15351, and is provided hereinbelow with reference to the sequence listing part.

[8202] VGAM589 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM589 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8203] An enzyme complex designated DICER COMPLEX, dices the VGAM589 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM589 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM589 RNA is designated SEQ ID:15352, and is provided hereinbelow with reference to the sequence listing part.

[8204] VGAM589 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM589 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM589 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[8205] VGAM589 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM589 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM589 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM589 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM589 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8206] The complementary binding of VGAM589 RNA, herein designated VGAM RNA, to host target binding sites on VGAM589 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM589 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM589 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8207] It is appreciated that VGAM589 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM589 host target genes. The mRNA of each one of this plurality of VGAM589 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM589 RNA, herein designated VGAM RNA, and which when bound by VGAM589 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM589 host target proteins.

[8208] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM589 gene, herein designated VGAM GENE, on one or

more VGAM589 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8209] It is yet further appreciated that a function of VGAM589 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM589 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM589 correlate with, and may be deduced from, the identity of the host target genes which VGAM589 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[8210] Nucleotide sequences of the VGAM589 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM589 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM589 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM589 are further described hereinbelow with reference to Table 1.

[8211] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM589 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8212] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 590 (VGAM590) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8213] VGAM590 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM590 was detected is described

hereinabove with reference to Figs. 2–8.

[8214] VGAM590 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A.

VGAM590 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8215] VGAM590 gene, herein designated VGAM GENE, encodes a VGAM590 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM590 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM590 precursor RNA is designated SEQ ID:15370, and is provided hereinbelow with reference to the sequence listing part.

[8216] VGAM590 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM590 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8217] An enzyme complex designated DICER COMPLEX, dices the VGAM590 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM590 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM590 RNA is designated SEQ ID:15371, and is provided hereinbelow with reference to the sequence listing part.

[8218] VGAM590 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM590 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM590 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8219] VGAM590 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM590 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM590 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM590 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM590 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8220] The complementary binding of VGAM590 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM590 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM590 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM590 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8221] It is appreciated that VGAM590 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM590 host target genes. The mRNA of each one of this plurality of VGAM590 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM590 RNA, herein designated VGAM RNA, and which when bound by VGAM590 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM590 host target proteins.

[8222] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM590 gene, herein designated VGAM GENE, on one or more VGAM590 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8223] It is yet further appreciated that a function of VGAM590 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM590 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM590 correlate with, and may be deduced from, the identity of the host target genes which VGAM590 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8224] Nucleotide sequences of the VGAM590 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM590 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM590 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM590 are further described hereinbelow with reference to Table 1.

[8225] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM590 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8226] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 591 (VGAM591) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8227] VGAM591 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM591 was detected is described hereinabove with reference to Figs. 2-8.

[8228] VGAM591 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM591 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8229] VGAM591 gene, herein designated VGAM GENE, encodes a VGAM591 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM591 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM591 precursor RNA is designated SEQ ID:15375, and is provided hereinbelow with reference to the sequence listing part.

[8230] VGAM591 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM591 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[8231] An enzyme complex designated DICER COMPLEX, dices the VGAM591 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM591 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM591 RNA is designated SEQ ID:15376, and is provided hereinbelow with reference to the sequence listing part.

[8232] VGAM591 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM591 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM591 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8233] VGAM591 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM591 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM591 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM591 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM591 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8234] The complementary binding of VGAM591 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM591 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM591 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM591 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8235] It is appreciated that VGAM591 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM591 host target genes. The mRNA of each one of this plurality of VGAM591 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM591 RNA, herein designated VGAM RNA, and which when bound by VGAM591 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM591 host target proteins.

[8236] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM591 gene, herein designated VGAM GENE, on one or more VGAM591 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8237] It is yet further appreciated that a function of VGAM591 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM591 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM591 correlate with, and may be deduced from, the identity of the host target genes which VGAM591 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8238] Nucleotide sequences of the VGAM591 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM591 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM591 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM591 are further described hereinbelow with reference to Table 1.

[8239] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM591 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8240] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 592 (VGAM592) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8241] VGAM592 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM592 was detected is described hereinabove with reference to Figs. 2-8.

[8242] VGAM592 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Sheeppox virus.

VGAM592 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8243] VGAM592 gene, herein designated VGAM GENE, encodes a VGAM592 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM592 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM592 precursor RNA is designated SEQ ID:15427, and is provided hereinbelow with reference to the sequence listing part.

[8244] VGAM592 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM592 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8245] An enzyme complex designated DICER COMPLEX, dices the VGAM592 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM592 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM592 RNA is designated SEQ ID:15428, and is provided hereinbelow with reference to the sequence listing part.

[8246] VGAM592 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM592 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM592 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8247] VGAM592 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM592 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM592 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM592 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM592 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8248] The complementary binding of VGAM592 RNA, herein designated VGAM RNA, to host target binding sites on VGAM592 host target RNA, herein designated VGAM HOST



TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM592 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM592 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8249] It is appreciated that VGAM592 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM592 host target genes. The mRNA of each one of this plurality of VGAM592 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM592 RNA, herein designated VGAM RNA, and which when bound by VGAM592 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM592 host target proteins.

[8250] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM592 gene, herein designated VGAM GENE, on one or more VGAM592 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8251] It is yet further appreciated that a function of VGAM592 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM592 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific functions, and accordingly utilities, of VGAM592 correlate with, and may be deduced from, the identity of the host target genes which VGAM592 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8252] Nucleotide sequences of the VGAM592 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM592 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM592 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM592 are further described hereinbelow with reference to Table 1.

[8253] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM592 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8254] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 593 (VGAM593) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8255] VGAM593 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM593 was detected is described hereinabove with reference to Figs. 2-8.

[8256] VGAM593 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3.

VGAM593 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8257] VGAM593 gene, herein designated VGAM GENE, encodes a VGAM593 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM593 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM593 precursor RNA is designated SEQ ID:15443, and is provided hereinbelow with reference to the sequence listing part.

[8258] VGAM593 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM593 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8259] An enzyme complex designated DICER COMPLEX, dices

the VGAM593 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM593 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM593 RNA is designated SEQ ID:15444, and is provided hereinbelow with reference to the sequence listing part.

[8260] VGAM593 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM593 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM593 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8261] VGAM593 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM593 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM593 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM593 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM593 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8262] The complementary binding of VGAM593 RNA, herein designated VGAM RNA, to host target binding sites on VGAM593 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM593 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM593 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8263] It is appreciated that VGAM593 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM593 host target genes. The mRNA of each one of this plurality of VGAM593 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM593 RNA, herein designated VGAM RNA, and which when bound by VGAM593 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM593 host target proteins.

[8264] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM593 gene, herein designated VGAM GENE, on one or more VGAM593 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8265] It is yet further appreciated that a function of VGAM593 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM593 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM593 correlate with, and may be deduced from, the identity of the host target genes which VGAM593 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8266] Nucleotide sequences of the VGAM593 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM593 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM593 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM593 are further described hereinbelow with reference to Table 1.

[8267] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM593 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8268] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 594 (VGAM594) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8269] VGAM594 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM594 was detected is described hereinabove with reference to Figs. 2-8.

[8270] VGAM594 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM594 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[8271] VGAM594 gene, herein designated VGAM GENE, encodes a VGAM594 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM594 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM594 precursor RNA is designated SEQ ID:15464, and is provided hereinbelow with reference to the sequence listing part.

[8272] VGAM594 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM594 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8273] An enzyme complex designated DICER COMPLEX, dices the VGAM594 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM594 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM594 RNA is designated SEQ ID:15465, and is provided hereinbelow with reference to the sequence listing part.

[8274] VGAM594 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM594 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM594 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8275] VGAM594 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM594 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM594 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM594 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM594 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8276] The complementary binding of VGAM594 RNA, herein designated VGAM RNA, to host target binding sites on VGAM594 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM594 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM594 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8277] It is appreciated that VGAM594 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM594 host target genes. The mRNA of each one of this plurality of VGAM594 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM594 RNA, herein designated VGAM RNA, and which when bound by VGAM594 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM594 host target proteins.

[8278] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM594 gene, herein designated VGAM GENE, on one or more VGAM594 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8279] It is yet further appreciated that a function of VGAM594 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM594 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM594 correlate with, and may be deduced from, the identity of the host target genes which VGAM594 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8280] Nucleotide sequences of the VGAM594 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM594 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM594 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM594 are further described hereinbelow with reference to Table 1.

[8281] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM594 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8282] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 595 (VGAM595) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8283] VGAM595 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM595 was detected is described hereinabove with reference to Figs. 2-8.

[8284] VGAM595 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox virus. VGAM595 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[8285] VGAM595 gene, herein designated VGAM GENE, encodes a VGAM595 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM595 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM595 precursor RNA is designated SEQ ID:15468, and is provided hereinbelow with reference to the sequence listing part.

[8286] VGAM595 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM595 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8287] An enzyme complex designated DICER COMPLEX, dices the VGAM595 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM595 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM595 RNA is designated SEQ ID:15469, and is provided hereinbelow with reference to the sequence listing part.

[8288] VGAM595 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM595 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM595 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8289] VGAM595 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM595 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM595 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM595 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM595 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8290] The complementary binding of VGAM595 RNA, herein designated VGAM RNA, to host target binding sites on VGAM595 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM595 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM595 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8291] It is appreciated that VGAM595 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM595 host target genes. The mRNA of each one of this plurality of VGAM595 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM595 RNA, herein designated VGAM RNA, and which when bound by VGAM595 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM595 host target proteins.

[8292] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM595 gene, herein designated VGAM GENE, on one or more VGAM595 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8293] It is yet further appreciated that a function of VGAM595 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM595 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific functions, and accordingly utilities, of VGAM595 correlate with, and may be deduced from, the identity of the host target genes which VGAM595 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8294] Nucleotide sequences of the VGAM595 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM595 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM595 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM595 are further de-

scribed hereinbelow with reference to Table 1.

[8295] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM595 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8296] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 596 (VGAM596) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8297] VGAM596 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM596 was detected is described hereinabove with reference to Figs. 2-8.

[8298] VGAM596 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM596 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8299] VGAM596 gene, herein designated VGAM GENE, encodes a VGAM596 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM596 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM596 precursor RNA is designated SEQ ID:15480, and is provided hereinbelow with reference to the sequence listing part.

[8300] VGAM596 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM596 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8301] An enzyme complex designated DICER COMPLEX, dices the VGAM596 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM596 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM596 RNA is designated SEQ ID:15481, and is provided hereinbelow with reference to the sequence listing part.

[8302] VGAM596 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM596 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM596 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8303] VGAM596 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM596 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM596 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM596 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM596 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8304] The complementary binding of VGAM596 RNA, herein designated VGAM RNA, to host target binding sites on VGAM596 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM596 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM596 host target protein, herein designated



VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8305] It is appreciated that VGAM596 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM596 host target genes. The mRNA of each one of this plurality of VGAM596 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM596 RNA, herein designated VGAM RNA, and which when bound by VGAM596 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM596 host target proteins.

[8306] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM596 gene, herein designated VGAM GENE, on one or more VGAM596 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8307] It is yet further appreciated that a function of VGAM596 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM596 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM596 correlate with, and may be deduced from, the identity of the host target genes which VGAM596 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8308] Nucleotide sequences of the VGAM596 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM596 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM596 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM596 are further described hereinbelow with reference to Table 1.

[8309] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM596 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8310] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 597 (VGAM597) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8311] VGAM597 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM597 was detected is described hereinabove with reference to Figs. 2-8.

[8312] VGAM597 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM597 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8313] VGAM597 gene, herein designated VGAM GENE, encodes a

VGAM597 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM597 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM597 precursor RNA is designated SEQ ID:15494, and is provided hereinbelow with reference to the sequence listing part.

[8314] VGAM597 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM597 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8315] An enzyme complex designated DICER COMPLEX, dices the VGAM597 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM597 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM597 RNA is designated SEQ ID:15495, and is provided hereinbelow with reference to the sequence listing part.

[8316] VGAM597 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM597 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM597 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8317] VGAM597 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM597 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM597 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM597 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM597 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8318] The complementary binding of VGAM597 RNA, herein designated VGAM RNA, to host target binding sites on VGAM597 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM597 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM597 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[8319] It is appreciated that VGAM597 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM597 host target genes. The mRNA of each one of this plurality of VGAM597 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM597 RNA, herein designated VGAM RNA, and which when bound by VGAM597 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM597 host target proteins.

[8320] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM597 gene, herein designated VGAM GENE, on one or more VGAM597 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8321] It is yet further appreciated that a function of VGAM597 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM597 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM597 correlate with, and may be deduced from, the identity of the host target genes which VGAM597 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8322] Nucleotide sequences of the VGAM597 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM597 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM597 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM597 are further described hereinbelow with reference to Table 1.

[8323] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM597 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8324] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 598 (VGAM598) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8325] VGAM598 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM598 was detected is described hereinabove with reference to Figs. 2-8.

[8326] VGAM598 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM598 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8327] VGAM598 gene, herein designated VGAM GENE, encodes a VGAM598 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM598 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM598 precursor RNA is designated SEQ ID:15498, and is provided hereinbelow with reference to the sequence listing part.

[8328] VGAM598 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM598 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8329] An enzyme complex designated DICER COMPLEX, dices the VGAM598 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM598 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM598 RNA is designated SEQ ID:15499, and is provided hereinbelow with reference to the sequence listing part.

[8330] VGAM598 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM598 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM598 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8331] VGAM598 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM598 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM598 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM598 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM598 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8332] The complementary binding of VGAM598 RNA, herein designated VGAM RNA, to host target binding sites on VGAM598 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM598 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM598 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8333] It is appreciated that VGAM598 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM598 host target genes. The mRNA of each one of this plurality of VGAM598 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM598 RNA, herein designated VGAM RNA, and which when bound by VGAM598 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM598 host target proteins.

[8334] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM598 gene, herein designated VGAM GENE, on one or more VGAM598 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8335] It is yet further appreciated that a function of VGAM598 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM598 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM598 correlate with, and may be deduced from, the identity of the host target genes which VGAM598 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8336] Nucleotide sequences of the VGAM598 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM598 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM598 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM598 are further described hereinbelow with reference to Table 1.

[8337] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM598 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8338] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 599 (VGAM599) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8339] VGAM599 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM599 was detected is described hereinabove with reference to Figs. 2–8.

[8340] VGAM599 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM599 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8341] VGAM599 gene, herein designated VGAM GENE, encodes a VGAM599 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM599 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM599 precursor RNA is designated SEQ ID:15503, and is provided hereinbelow with reference to the sequence listing part.

[8342] VGAM599 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM599 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8343] An enzyme complex designated DICER COMPLEX, dices the VGAM599 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM599 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM599 RNA is designated SEQ ID:15504, and is provided hereinbelow with reference to the sequence listing part.

[8344] VGAM599 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM599 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM599 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8345] VGAM599 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM599 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM599 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM599 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM599 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8346] The complementary binding of VGAM599 RNA, herein designated VGAM RNA, to host target binding sites on VGAM599 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM599 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM599 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8347] It is appreciated that VGAM599 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM599 host target genes. The mRNA of each one of this plurality of VGAM599 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM599 RNA, herein designated VGAM RNA, and which when bound by VGAM599 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM599 host target proteins.

[8348] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM599 gene, herein designated VGAM GENE, on one or more VGAM599 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8349] It is yet further appreciated that a function of VGAM599 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM599 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM599 correlate with, and may be deduced from, the identity of the host target genes which VGAM599 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8350] Nucleotide sequences of the VGAM599 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM599 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM599 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM599 are further described hereinbelow with reference to Table 1.

[8351] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM599 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8352] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 600 (VGAM600) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8353] VGAM600 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM600 was detected is described hereinabove with reference to Figs. 2–8.

[8354] VGAM600 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM600 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8355] VGAM600 gene, herein designated VGAM GENE, encodes a VGAM600 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM600 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM600 precursor RNA is designated SEQ ID:15536, and is provided hereinbelow with reference to the sequence listing part.

[8356] VGAM600 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM600 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8357] An enzyme complex designated DICER COMPLEX, dices the VGAM600 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM600 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM600 RNA is designated SEQ ID:15537, and is provided hereinbelow with reference to the sequence listing part.

[8358] VGAM600 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM600 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM600 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8359] VGAM600 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM600 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM600 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM600 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM600 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8360] The complementary binding of VGAM600 RNA, herein designated VGAM RNA, to host target binding sites on VGAM600 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM600 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM600 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8361] It is appreciated that VGAM600 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM600 host target genes. The mRNA of each one of this plurality of VGAM600 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM600 RNA, herein designated VGAM RNA, and which when bound by VGAM600 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM600 host target proteins.

[8362] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM600 gene, herein designated VGAM GENE, on one or more VGAM600 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[8363] It is yet further appreciated that a function of VGAM600 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM600 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM600 correlate with, and may be deduced from, the identity of the host target genes which VGAM600 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8364] Nucleotide sequences of the VGAM600 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM600 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM600 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM600 are further described hereinbelow with reference to Table 1.

[8365] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM600 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8366] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 601 (VGAM601) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8367] VGAM601 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM601 was detected is described hereinabove with reference to Figs. 2–8.

[8368] VGAM601 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus C. VGAM601 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8369] VGAM601 gene, herein designated VGAM GENE, encodes a VGAM601 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM601 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM601 precursor RNA is designated SEQ ID:15548, and is provided hereinbelow with reference to the sequence listing part.

[8370] VGAM601 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM601 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8371] An enzyme complex designated DICER COMPLEX, dices the VGAM601 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM601 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM601 RNA is designated SEQ ID:15549, and is provided hereinbelow with reference to the sequence listing part.

[8372] VGAM601 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM601 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM601 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8373] VGAM601 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM601 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM601 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM601 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM601 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8374] The complementary binding of VGAM601 RNA, herein designated VGAM RNA, to host target binding sites on VGAM601 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM601 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM601 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8375] It is appreciated that VGAM601 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM601 host target genes. The mRNA of

each one of this plurality of VGAM601 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM601 RNA, herein designated VGAM RNA, and which when bound by VGAM601 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM601 host target proteins.

[8376] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM601 gene, herein designated VGAM GENE, on one or more VGAM601 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[8377] It is yet further appreciated that a function of VGAM601 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM601 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus C. Specific functions, and accordingly utilities, of VGAM601 correlate with, and may be deduced from, the identity of the host target genes which VGAM601 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8378] Nucleotide sequences of the VGAM601 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM601 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM601 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM601 are further described hereinbelow with reference to Table 1.

[8379] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM601 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[8380] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 602 (VGAM602) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8381] VGAM602 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM602 was detected is described hereinabove with reference to Figs. 2–8.

[8382] VGAM602 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM602 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8383] VGAM602 gene, herein designated VGAM GENE, encodes a VGAM602 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM602 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM602 precursor RNA is designated SEQ ID:15605, and is provided hereinbelow with reference to the sequence listing part.

[8384] VGAM602 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM602 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8385] An enzyme complex designated DICER COMPLEX, dices the VGAM602 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM602 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM602 RNA is designated SEQ ID:15606, and

is provided hereinbelow with reference to the sequence listing part.

[8386] VGAM602 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM602 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM602 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8387] VGAM602 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM602 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM602 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM602 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM602 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8388] The complementary binding of VGAM602 RNA, herein designated VGAM RNA, to host target binding sites on VGAM602 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM602 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM602 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8389] It is appreciated that VGAM602 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM602 host target genes. The mRNA of each one of this plurality of VGAM602 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM602 RNA, herein designated VGAM RNA, and which when bound by VGAM602 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM602 host target proteins.

[8390] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM602 gene, herein designated VGAM GENE, on one or more VGAM602 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8391] It is yet further appreciated that a function of VGAM602 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM602 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM602 correlate with, and may be deduced from, the identity of the host target genes which VGAM602 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8392] Nucleotide sequences of the VGAM602 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM602 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM602 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM602 are further described hereinbelow with reference to Table 1.

[8393] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM602 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8394] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 603 (VGAM603) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8395] VGAM603 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM603 was detected is described hereinabove with reference to Figs. 2–8.

[8396] VGAM603 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM603 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8397] VGAM603 gene, herein designated VGAM GENE, encodes a VGAM603 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM603 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM603 precursor RNA is

designated SEQ ID:15626, and is provided hereinbelow with reference to the sequence listing part.

[8398] VGAM603 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM603 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8399] An enzyme complex designated DICER COMPLEX, dices the VGAM603 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM603 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM603 RNA is designated SEQ ID:15627, and is provided hereinbelow with reference to the sequence



listing part.

[8400] VGAM603 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM603 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM603 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8401] VGAM603 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM603 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM603 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM603 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM603 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8402] The complementary binding of VGAM603 RNA, herein designated VGAM RNA, to host target binding sites on VGAM603 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM603 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM603 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8403] It is appreciated that VGAM603 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM603 host target genes. The mRNA of each one of this plurality of VGAM603 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM603 RNA, herein designated VGAM RNA, and which when bound by VGAM603 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM603 host target proteins.

[8404] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM603 gene, herein designated VGAM GENE, on one or more VGAM603 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8405] It is yet further appreciated that a function of VGAM603 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM603 include diagnosis, prevention and treatment of viral infection by *Amsacta moorei* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM603 correlate with, and may be deduced from, the identity of the host target genes which VGAM603 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8406] Nucleotide sequences of the VGAM603 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM603 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM603 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM603 are further described hereinbelow with reference to Table 1.

[8407] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM603 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8408] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 604 (VGAM604) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8409] VGAM604 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM604 was detected is described hereinabove with reference to Figs. 2–8.

[8410] VGAM604 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM604 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8411] VGAM604 gene, herein designated VGAM GENE, encodes a VGAM604 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM604 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM604 precursor RNA is designated SEQ ID:15631, and is provided hereinbelow

with reference to the sequence listing part.

[8412] VGAM604 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM604 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8413] An enzyme complex designated DICER COMPLEX, dices the VGAM604 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM604 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM604 RNA is designated SEQ ID:15632, and is provided hereinbelow with reference to the sequence listing part.

[8414] VGAM604 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM604 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM604 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8415] VGAM604 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM604 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM604 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM604 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM604 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8416] The complementary binding of VGAM604 RNA, herein designated VGAM RNA, to host target binding sites on VGAM604 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM604 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM604 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8417] It is appreciated that VGAM604 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM604 host target genes. The mRNA of each one of this plurality of VGAM604 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM604 RNA, herein designated VGAM RNA, and which when bound by VGAM604 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM604 host target proteins.

[8418] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM604 gene, herein designated VGAM GENE, on one or more VGAM604 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8419] It is yet further appreciated that a function of VGAM604 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM604 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM604 correlate with, and may be deduced from, the identity of the host target genes which VGAM604 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8420] Nucleotide sequences of the VGAM604 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM604 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM604 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM604 are further described hereinbelow with reference to Table 1.

[8421] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM604 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8422] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 605 (VGAM605) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8423] VGAM605 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM605 was detected is described hereinabove with reference to Figs. 2–8.

[8424] VGAM605 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM605 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8425] VGAM605 gene, herein designated VGAM GENE, encodes a VGAM605 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM605 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM605 precursor RNA is designated SEQ ID:15701, and is provided hereinbelow with reference to the sequence listing part.

[8426] VGAM605 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM605 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8427] An enzyme complex designated DICER COMPLEX, dices the VGAM605 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM605 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM605 RNA is designated SEQ ID:15702, and is provided hereinbelow with reference to the sequence listing part.

[8428] VGAM605 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM605 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM605 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8429] VGAM605 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM605 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM605 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM605 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM605 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8430] The complementary binding of VGAM605 RNA, herein designated VGAM RNA, to host target binding sites on VGAM605 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM605 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM605 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8431] It is appreciated that VGAM605 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM605 host target genes. The mRNA of each one of this plurality of VGAM605 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM605 RNA, herein designated VGAM

RNA, and which when bound by VGAM605 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM605 host target proteins.

[8432] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM605 gene, herein designated VGAM GENE, on one or more VGAM605 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8433] It is yet further appreciated that a function of VGAM605 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM605 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM605 correlate with, and may be deduced from, the identity of the host target genes which VGAM605 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8434] Nucleotide sequences of the VGAM605 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM605 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM605 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM605 are further described hereinbelow with reference to Table 1.

[8435] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM605 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8436] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 606 (VGAM606) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8437] VGAM606 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM606 was detected is described hereinabove with reference to Figs. 2-8.

[8438] VGAM606 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV-2. VGAM606 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8439] VGAM606 gene, herein designated VGAM GENE, encodes a VGAM606 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM606 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM606 precursor RNA is designated SEQ ID:15717, and is provided hereinbelow with reference to the sequence listing part.

[8440] VGAM606 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM606 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8441] An enzyme complex designated DICER COMPLEX, dices the VGAM606 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM606 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM606 RNA is designated SEQ ID:15718, and is provided hereinbelow with reference to the sequence listing part.

[8442] VGAM606 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM606 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM606 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8443] VGAM606 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM606 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM606 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM606 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM606 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8444] The complementary binding of VGAM606 RNA, herein designated VGAM RNA, to host target binding sites on VGAM606 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM606 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM606 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8445] It is appreciated that VGAM606 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM606 host target genes. The mRNA of each one of this plurality of VGAM606 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM606 RNA, herein designated VGAM RNA, and which when bound by VGAM606 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM606 host target proteins.

[8446] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM606 gene, herein designated VGAM GENE, on one or more VGAM606 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8447] It is yet further appreciated that a function of VGAM606 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM606 include diagnosis, prevention and

treatment of viral infection by Sulfolobus virus SIRV-2. Specific functions, and accordingly utilities, of VGAM606 correlate with, and may be deduced from, the identity of the host target genes which VGAM606 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8448] Nucleotide sequences of the VGAM606 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM606 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM606 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM606 are further described hereinbelow with reference to Table 1.

[8449] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM606 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8450] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 607 (VGAM607) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8451] VGAM607 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM607 was detected is described hereinabove with reference to Figs. 2–8.

[8452] VGAM607 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM607 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8453] VGAM607 gene, herein designated VGAM GENE, encodes a VGAM607 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM607 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM607 precursor RNA is designated SEQ ID:15726, and is provided hereinbelow with reference to the sequence listing part.

[8454] VGAM607 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM607 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8455] An enzyme complex designated DICER COMPLEX, dices the VGAM607 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM607 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM607 RNA is designated SEQ ID:15727, and is provided hereinbelow with reference to the sequence listing part.

[8456] VGAM607 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM607 host target RNA, herein designated VGAM



HOST TARGET RNA. VGAM607 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8457] VGAM607 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM607 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM607 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM607 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM607 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8458] The complementary binding of VGAM607 RNA, herein designated VGAM RNA, to host target binding sites on VGAM607 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM607 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM607 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8459] It is appreciated that VGAM607 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM607 host target genes. The mRNA of each one of this plurality of VGAM607 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM607 RNA, herein designated VGAM RNA, and which when bound by VGAM607 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM607 host target proteins.

[8460] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM607 gene, herein designated VGAM GENE, on one or more VGAM607 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8461] It is yet further appreciated that a function of VGAM607 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM607 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific

functions, and accordingly utilities, of VGAM607 correlate with, and may be deduced from, the identity of the host target genes which VGAM607 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8462] Nucleotide sequences of the VGAM607 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM607 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM607 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM607 are further described hereinbelow with reference to Table 1.

[8463] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM607 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8464] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 608 (VGAM608) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[8465] VGAM608 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM608 was detected is described hereinabove with reference to Figs. 2–8.

[8466] VGAM608 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM608 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8467] VGAM608 gene, herein designated VGAM GENE, encodes a VGAM608 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM608 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM608 precursor RNA is designated SEQ ID:15766, and is provided hereinbelow with reference to the sequence listing part.

[8468] VGAM608 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM608 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8469] An enzyme complex designated DICER COMPLEX, dices the VGAM608 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM608 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM608 RNA is designated SEQ ID:15767, and is provided hereinbelow with reference to the sequence listing part.

[8470] VGAM608 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM608 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM608 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8471] VGAM608 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM608 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM608 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM608 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM608 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8472] The complementary binding of VGAM608 RNA, herein designated VGAM RNA, to host target binding sites on VGAM608 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM608 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM608 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8473] It is appreciated that VGAM608 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM608 host target genes. The mRNA of each one of this plurality of VGAM608 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM608 RNA, herein designated VGAM RNA, and which when bound by VGAM608 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM608 host target proteins.



[8474] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM608 gene, herein designated VGAM GENE, on one or more VGAM608 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8475] It is yet further appreciated that a function of VGAM608 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM608 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM608 correlate

with, and may be deduced from, the identity of the host target genes which VGAM608 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8476] Nucleotide sequences of the VGAM608 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM608 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM608 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM608 are further described hereinbelow with reference to Table 1.

[8477] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM608 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8478] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 609 (VGAM609) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[8479] VGAM609 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM609 was detected is described hereinabove with reference to Figs. 2–8.

[8480] VGAM609 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola virus. VGAM609 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8481] VGAM609 gene, herein designated VGAM GENE, encodes a VGAM609 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM609 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM609 precursor RNA is designated SEQ ID:15777, and is provided hereinbelow with reference to the sequence listing part.

[8482] VGAM609 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM609 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8483] An enzyme complex designated DICER COMPLEX, dices the VGAM609 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM609 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM609 RNA is designated SEQ ID:15778, and is provided hereinbelow with reference to the sequence listing part.

[8484] VGAM609 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM609 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM609 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8485] VGAM609 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM609 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM609 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM609 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM609 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8486] The complementary binding of VGAM609 RNA, herein designated VGAM RNA, to host target binding sites on VGAM609 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM609 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM609 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8487] It is appreciated that VGAM609 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM609 host target genes. The mRNA of each one of this plurality of VGAM609 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM609 RNA, herein designated VGAM RNA, and which when bound by VGAM609 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM609 host target proteins.

[8488] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM609 gene, herein designated VGAM GENE, on one or more VGAM609 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8489] It is yet further appreciated that a function of VGAM609 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM609 include diagnosis, prevention and treatment of viral infection by Variola virus. Specific functions, and accordingly utilities, of VGAM609 correlate with, and may be deduced from, the identity of the host target genes which VGAM609 binds and inhibits, and the

function of these host target genes, as elaborated herein—below.

[8490] Nucleotide sequences of the VGAM609 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM609 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM609 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM609 are further described hereinbelow with reference to Table 1.

[8491] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM609 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8492] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 610 (VGAM610) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8493] VGAM610 is a novel bioinformatically detected regulatory,



non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM610 was detected is described hereinabove with reference to Figs. 2–8.

[8494] VGAM610 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM610 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8495] VGAM610 gene, herein designated VGAM GENE, encodes a VGAM610 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM610 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM610 precursor RNA is designated SEQ ID:15784, and is provided hereinbelow with reference to the sequence listing part.

[8496] VGAM610 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM610 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8497] An enzyme complex designated DICER COMPLEX, dices the VGAM610 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM610 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM610 RNA is designated SEQ ID:15785, and is provided hereinbelow with reference to the sequence listing part.

[8498] VGAM610 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM610 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM610 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8499] VGAM610 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM610 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM610 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM610 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM610 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[8500] The complementary binding of VGAM610 RNA, herein designated VGAM RNA, to host target binding sites on VGAM610 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM610 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM610 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8501] It is appreciated that VGAM610 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM610 host target genes. The mRNA of each one of this plurality of VGAM610 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM610 RNA, herein designated VGAM RNA, and which when bound by VGAM610 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM610 host target proteins.

[8502] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM610 gene, herein designated VGAM GENE, on one or more VGAM610 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8503] It is yet further appreciated that a function of VGAM610 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM610 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM610 correlate with, and may be deduced from, the identity of the host target genes which VGAM610 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[8504] Nucleotide sequences of the VGAM610 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM610 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM610 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM610 are further described hereinbelow with reference to Table 1.

[8505] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM610 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8506] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 611 (VGAM611) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8507] VGAM611 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM611 was detected is described hereinabove with reference to Figs. 2–8.

[8508] VGAM611 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM611 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8509] VGAM611 gene, herein designated VGAM GENE, encodes a VGAM611 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM611 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM611 precursor RNA is designated SEQ ID:15794, and is provided hereinbelow with reference to the sequence listing part.

[8510] VGAM611 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM611 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8511] An enzyme complex designated DICER COMPLEX, dices the VGAM611 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM611 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM611 RNA is designated SEQ ID:15795, and is provided hereinbelow with reference to the sequence listing part.

[8512] VGAM611 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM611 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM611 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and



3UTR respectively.

[8513] VGAM611 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM611 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM611 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM611 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM611 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8514] The complementary binding of VGAM611 RNA, herein designated VGAM RNA, to host target binding sites on VGAM611 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM611 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM611 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8515] It is appreciated that VGAM611 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM611 host target genes. The mRNA of each one of this plurality of VGAM611 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM611 RNA, herein designated VGAM RNA, and which when bound by VGAM611 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM611 host target proteins.

[8516] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM611 gene, herein designated VGAM GENE, on one or

more VGAM611 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8517] It is yet further appreciated that a function of VGAM611 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM611 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM611 correlate with, and may be deduced from, the identity of the host target genes which VGAM611 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8518] Nucleotide sequences of the VGAM611 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM611 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM611 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM611 are further described hereinbelow with reference to Table 1.

[8519] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM611 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8520] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 612 (VGAM612) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8521] VGAM612 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM612 was detected is described

hereinabove with reference to Figs. 2–8.

[8522] VGAM612 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus.

VGAM612 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8523] VGAM612 gene, herein designated VGAM GENE, encodes a VGAM612 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM612 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM612 precursor RNA is designated SEQ ID:15797, and is provided hereinbelow with reference to the sequence listing part.

[8524] VGAM612 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM612 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8525] An enzyme complex designated DICER COMPLEX, dices the VGAM612 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM612 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM612 RNA is designated SEQ ID:15798, and is provided hereinbelow with reference to the sequence listing part.

[8526] VGAM612 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM612 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM612 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8527] VGAM612 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM612 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM612 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM612 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM612 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8528] The complementary binding of VGAM612 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM612 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM612 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM612 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8529] It is appreciated that VGAM612 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM612 host target genes. The mRNA of each one of this plurality of VGAM612 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM612 RNA, herein designated VGAM RNA, and which when bound by VGAM612 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM612 host target proteins.

[8530] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM612 gene, herein designated VGAM GENE, on one or more VGAM612 host target gene, herein designated



VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8531] It is yet further appreciated that a function of VGAM612 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM612 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM612 correlate with, and may be deduced from, the identity of the host target genes which VGAM612 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8532] Nucleotide sequences of the VGAM612 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM612 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM612 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM612 are further described hereinbelow with reference to Table 1.

[8533] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM612 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8534] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 613 (VGAM613) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8535] VGAM613 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM613 was detected is described hereinabove with reference to Figs. 2-8.

[8536] VGAM613 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM613 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8537] VGAM613 gene, herein designated VGAM GENE, encodes a VGAM613 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM613 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM613 precursor RNA is designated SEQ ID:15864, and is provided hereinbelow with reference to the sequence listing part.

[8538] VGAM613 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM613 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[8539] An enzyme complex designated DICER COMPLEX, dices the VGAM613 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM613 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM613 RNA is designated SEQ ID:15865, and is provided hereinbelow with reference to the sequence listing part.

[8540] VGAM613 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM613 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM613 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8541] VGAM613 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM613 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM613 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM613 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM613 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8542] The complementary binding of VGAM613 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM613 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM613 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM613 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8543] It is appreciated that VGAM613 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM613 host target genes. The mRNA of each one of this plurality of VGAM613 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM613 RNA, herein designated VGAM RNA, and which when bound by VGAM613 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM613 host target proteins.

[8544] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM613 gene, herein designated VGAM GENE, on one or more VGAM613 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8545] It is yet further appreciated that a function of VGAM613 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM613 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM613 correlate with, and may be deduced from, the identity of the host target genes which VGAM613 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8546] Nucleotide sequences of the VGAM613 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM613 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM613 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM613 are further described hereinbelow with reference to Table 1.

[8547] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM613 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8548] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 614 (VGAM614) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8549] VGAM614 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM614 was detected is described hereinabove with reference to Figs. 2-8.

[8550] VGAM614 gene, herein designated VGAM GENE, is a viral



gene contained in the genome of Human herpesvirus 5. VGAM614 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8551] VGAM614 gene, herein designated VGAM GENE, encodes a VGAM614 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM614 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM614 precursor RNA is designated SEQ ID:15867, and is provided hereinbelow with reference to the sequence listing part.

[8552] VGAM614 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM614 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8553] An enzyme complex designated DICER COMPLEX, dices the VGAM614 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM614 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM614 RNA is designated SEQ ID:15868, and is provided hereinbelow with reference to the sequence listing part.

[8554] VGAM614 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM614 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM614 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8555] VGAM614 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM614 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM614 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM614 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM614 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8556] The complementary binding of VGAM614 RNA, herein designated VGAM RNA, to host target binding sites on VGAM614 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM614 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM614 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8557] It is appreciated that VGAM614 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM614 host target genes. The mRNA of each one of this plurality of VGAM614 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM614 RNA, herein designated VGAM RNA, and which when bound by VGAM614 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM614 host target proteins.

[8558] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM614 gene, herein designated VGAM GENE, on one or more VGAM614 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8559] It is yet further appreciated that a function of VGAM614 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM614 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM614 correlate with, and may be deduced from, the identity of the host target genes which VGAM614 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8560] Nucleotide sequences of the VGAM614 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM614 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM614 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM614 are further described hereinbelow with reference to Table 1.

[8561] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM614 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8562]

[8563] Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 615 (VGAM615) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8564] VGAM615 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM615 was detected is described hereinabove with reference to Figs. 2-8.

[8565] VGAM615 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5.

VGAM615 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8566] VGAM615 gene, herein designated VGAM GENE, encodes a VGAM615 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM615 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM615 precursor RNA is designated SEQ ID:15890, and is provided hereinbelow with reference to the sequence listing part.

[8567] VGAM615 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM615 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8568] An enzyme complex designated DICER COMPLEX, dices

the VGAM615 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM615 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM615 RNA is designated SEQ ID:15891, and is provided hereinbelow with reference to the sequence listing part.

[8569] VGAM615 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM615 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM615 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8570] VGAM615 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM615 host target



RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM615 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM615 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM615 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8571] The complementary binding of VGAM615 RNA, herein designated VGAM RNA, to host target binding sites on VGAM615 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM615 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM615 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8572] It is appreciated that VGAM615 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM615 host target genes. The mRNA of each one of this plurality of VGAM615 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM615 RNA, herein designated VGAM RNA, and which when bound by VGAM615 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM615 host target proteins.

[8573] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM615 gene, herein designated VGAM GENE, on one or more VGAM615 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8574] It is yet further appreciated that a function of VGAM615 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM615 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM615 correlate with, and may be deduced from, the identity of the host target genes which VGAM615 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8575] Nucleotide sequences of the VGAM615 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM615 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM615 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM615 are further described hereinbelow with reference to Table 1.

[8576] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM615 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8577] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 616 (VGAM616) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8578] VGAM616 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM616 was detected is described hereinabove with reference to Figs. 2-8.

[8579] VGAM616 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM616 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8580] VGAM616 gene, herein designated VGAM GENE, encodes a VGAM616 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM616 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM616 precursor RNA is designated SEQ ID:15894, and is provided hereinbelow with reference to the sequence listing part.

[8581] VGAM616 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM616 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8582] An enzyme complex designated DICER COMPLEX, dices the VGAM616 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM616 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM616 RNA is designated SEQ ID:15895, and is provided hereinbelow with reference to the sequence listing part.

[8583] VGAM616 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM616 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM616 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8584] VGAM616 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM616 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM616 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM616 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM616 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8585] The complementary binding of VGAM616 RNA, herein designated VGAM RNA, to host target binding sites on VGAM616 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM616 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM616 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8586] It is appreciated that VGAM616 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM616 host target genes. The mRNA of each one of this plurality of VGAM616 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM616 RNA, herein designated VGAM RNA, and which when bound by VGAM616 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM616 host target proteins.

[8587] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM616 gene, herein designated VGAM GENE, on one or more VGAM616 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated



only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8588] It is yet further appreciated that a function of VGAM616 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM616 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM616 correlate with, and may be deduced from, the identity of the host target genes which VGAM616 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8589] Nucleotide sequences of the VGAM616 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM616 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM616 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM616 are further described hereinbelow with reference to Table 1.

[8590] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM616 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8591] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 617 (VGAM617) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8592] VGAM617 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM617 was detected is described hereinabove with reference to Figs. 2-8.

[8593] VGAM617 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM617 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[8594] VGAM617 gene, herein designated VGAM GENE, encodes a VGAM617 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM617 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM617 precursor RNA is designated SEQ ID:15904, and is provided hereinbelow with reference to the sequence listing part.

[8595] VGAM617 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM617 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8596] An enzyme complex designated DICER COMPLEX, dices the VGAM617 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM617 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM617 RNA is designated SEQ ID:15905, and is provided hereinbelow with reference to the sequence listing part.

[8597] VGAM617 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM617 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM617 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8598] VGAM617 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM617 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM617 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM617 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM617 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8599] The complementary binding of VGAM617 RNA, herein designated VGAM RNA, to host target binding sites on VGAM617 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM617 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM617 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8600] It is appreciated that VGAM617 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM617 host target genes. The mRNA of each one of this plurality of VGAM617 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM617 RNA, herein designated VGAM RNA, and which when bound by VGAM617 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM617 host target proteins.

[8601] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM617 gene, herein designated VGAM GENE, on one or more VGAM617 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8602] It is yet further appreciated that a function of VGAM617 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM617 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM617 correlate with, and may be deduced from, the identity of the host target genes which VGAM617 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8603] Nucleotide sequences of the VGAM617 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM617 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM617 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM617 are further de-

scribed hereinbelow with reference to Table 1.

[8604] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM617 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8605] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 618 (VGAM618) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8606] VGAM618 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM618 was detected is described hereinabove with reference to Figs. 2-8.

[8607] VGAM618 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM618 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.



[8608] VGAM618 gene, herein designated VGAM GENE, encodes a VGAM618 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM618 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM618 precursor RNA is designated SEQ ID:15911, and is provided hereinbelow with reference to the sequence listing part.

[8609] VGAM618 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM618 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8610] An enzyme complex designated DICER COMPLEX, dices the VGAM618 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM618 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM618 RNA is designated SEQ ID:15912, and is provided hereinbelow with reference to the sequence listing part.

[8611] VGAM618 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM618 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM618 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8612] VGAM618 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM618 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM618 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM618 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM618 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8613] The complementary binding of VGAM618 RNA, herein designated VGAM RNA, to host target binding sites on VGAM618 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM618 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM618 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8614] It is appreciated that VGAM618 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM618 host target genes. The mRNA of each one of this plurality of VGAM618 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM618 RNA, herein designated VGAM RNA, and which when bound by VGAM618 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM618 host target proteins.

[8615] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM618 gene, herein designated VGAM GENE, on one or more VGAM618 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8616] It is yet further appreciated that a function of VGAM618 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM618 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM618 correlate with, and may be deduced from, the identity of the host target genes which VGAM618 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8617] Nucleotide sequences of the VGAM618 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM618 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM618 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM618 are further described hereinbelow with reference to Table 1.

[8618] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM618 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8619] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 619 (VGAM619) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8620] VGAM619 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM619 was detected is described hereinabove with reference to Figs. 2-8.

[8621] VGAM619 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM619 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8622] VGAM619 gene, herein designated VGAM GENE, encodes a

VGAM619 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM619 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM619 precursor RNA is designated SEQ ID:15922, and is provided hereinbelow with reference to the sequence listing part.

[8623] VGAM619 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM619 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8624] An enzyme complex designated DICER COMPLEX, dices the VGAM619 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM619 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM619 RNA is designated SEQ ID:15923, and is provided hereinbelow with reference to the sequence listing part.

[8625] VGAM619 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM619 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM619 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8626] VGAM619 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM619 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM619 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed



sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM619 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM619 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8627] The complementary binding of VGAM619 RNA, herein designated VGAM RNA, to host target binding sites on VGAM619 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM619 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM619 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[8628] It is appreciated that VGAM619 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM619 host target genes. The mRNA of each one of this plurality of VGAM619 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM619 RNA, herein designated VGAM RNA, and which when bound by VGAM619 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM619 host target proteins.

[8629] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM619 gene, herein designated VGAM GENE, on one or more VGAM619 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8630] It is yet further appreciated that a function of VGAM619 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM619 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM619 correlate with, and may be deduced from, the identity of the host target genes which VGAM619 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8631] Nucleotide sequences of the VGAM619 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM619 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM619 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM619 are further described hereinbelow with reference to Table 1.

[8632] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM619 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8633] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 620 (VGAM620) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8634] VGAM620 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM620 was detected is described hereinabove with reference to Figs. 2-8.

[8635] VGAM620 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM620 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8636] VGAM620 gene, herein designated VGAM GENE, encodes a VGAM620 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM620 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM620 precursor RNA is designated SEQ ID:15939, and is provided hereinbelow with reference to the sequence listing part.

[8637] VGAM620 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM620 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8638] An enzyme complex designated DICER COMPLEX, dices the VGAM620 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM620 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM620 RNA is designated SEQ ID:15940, and is provided hereinbelow with reference to the sequence listing part.

[8639] VGAM620 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM620 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM620 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8640] VGAM620 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM620 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM620 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM620 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM620 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8641] The complementary binding of VGAM620 RNA, herein designated VGAM RNA, to host target binding sites on VGAM620 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM620 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM620 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8642] It is appreciated that VGAM620 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM620 host target genes. The mRNA of each one of this plurality of VGAM620 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM620 RNA, herein designated VGAM RNA, and which when bound by VGAM620 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM620 host target proteins.

[8643] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM620 gene, herein designated VGAM GENE, on one or more VGAM620 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-



though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8644] It is yet further appreciated that a function of VGAM620 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM620 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM620 correlate with, and may be deduced from, the identity of the host target genes which VGAM620 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8645] Nucleotide sequences of the VGAM620 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM620 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM620 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM620 are further described hereinbelow with reference to Table 1.

[8646] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM620 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8647] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 621 (VGAM621) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8648] VGAM621 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM621 was detected is described hereinabove with reference to Figs. 2–8.

[8649] VGAM621 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM621 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8650] VGAM621 gene, herein designated VGAM GENE, encodes a VGAM621 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM621 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM621 precursor RNA is designated SEQ ID:15949, and is provided hereinbelow with reference to the sequence listing part.

[8651] VGAM621 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM621 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8652] An enzyme complex designated DICER COMPLEX, dices the VGAM621 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM621 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM621 RNA is designated SEQ ID:15950, and is provided hereinbelow with reference to the sequence listing part.

[8653] VGAM621 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM621 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM621 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8654] VGAM621 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM621 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM621 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM621 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM621 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8655] The complementary binding of VGAM621 RNA, herein designated VGAM RNA, to host target binding sites on VGAM621 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM621 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM621 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8656] It is appreciated that VGAM621 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM621 host target genes. The mRNA of each one of this plurality of VGAM621 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM621 RNA, herein designated VGAM RNA, and which when bound by VGAM621 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM621 host target proteins.

[8657] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM621 gene, herein designated VGAM GENE, on one or more VGAM621 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8658] It is yet further appreciated that a function of VGAM621 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM621 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM621 correlate with, and may be deduced from, the identity of the host target genes which VGAM621 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8659] Nucleotide sequences of the VGAM621 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM621 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM621 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM621 are further described hereinbelow with reference to Table 1.

[8660] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM621 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8661] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 622 (VGAM622) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8662] VGAM622 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM622 was detected is described hereinabove with reference to Figs. 2–8.

[8663] VGAM622 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM622 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8664] VGAM622 gene, herein designated VGAM GENE, encodes a VGAM622 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM622 precursor RNA, herein



designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM622 precursor RNA is designated SEQ ID:15960, and is provided hereinbelow with reference to the sequence listing part.

[8665] VGAM622 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM622 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8666] An enzyme complex designated DICER COMPLEX, dices the VGAM622 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM622 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM622 RNA is designated SEQ ID:15961, and is provided hereinbelow with reference to the sequence listing part.

[8667] VGAM622 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM622 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM622 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8668] VGAM622 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM622 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM622 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM622 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM622 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8669] The complementary binding of VGAM622 RNA, herein designated VGAM RNA, to host target binding sites on VGAM622 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM622 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM622 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8670] It is appreciated that VGAM622 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM622 host target genes. The mRNA of each one of this plurality of VGAM622 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM622 RNA, herein designated VGAM RNA, and which when bound by VGAM622 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM622 host target proteins.

[8671] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM622 gene, herein designated VGAM GENE, on one or more VGAM622 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[8672] It is yet further appreciated that a function of VGAM622 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM622 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM622 correlate with, and may be deduced from, the identity of the host target genes which VGAM622 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8673] Nucleotide sequences of the VGAM622 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM622 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM622 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM622 are further described hereinbelow with reference to Table 1.

[8674] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM622 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8675] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 623 (VGAM623) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8676] VGAM623 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM623 was detected is described hereinabove with reference to Figs. 2–8.

[8677] VGAM623 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM623 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8678] VGAM623 gene, herein designated VGAM GENE, encodes a VGAM623 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM623 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM623 precursor RNA is designated SEQ ID:15967, and is provided hereinbelow with reference to the sequence listing part.

[8679] VGAM623 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM623 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8680] An enzyme complex designated DICER COMPLEX, dices the VGAM623 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM623 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM623 RNA is designated SEQ ID:15968, and is provided hereinbelow with reference to the sequence listing part.

[8681] VGAM623 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM623 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM623 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8682] VGAM623 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM623 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM623 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-



preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM623 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM623 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8683] The complementary binding of VGAM623 RNA, herein designated VGAM RNA, to host target binding sites on VGAM623 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM623 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM623 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8684] It is appreciated that VGAM623 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM623 host target genes. The mRNA of

each one of this plurality of VGAM623 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM623 RNA, herein designated VGAM RNA, and which when bound by VGAM623 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM623 host target proteins.

[8685] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM623 gene, herein designated VGAM GENE, on one or more VGAM623 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[8686] It is yet further appreciated that a function of VGAM623 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM623 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM623 correlate with, and may be deduced from, the identity of the host target genes which VGAM623 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8687] Nucleotide sequences of the VGAM623 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM623 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM623 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM623 are further described hereinbelow with reference to Table 1.

[8688] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM623 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[8689] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 624 (VGAM624) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8690] VGAM624 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM624 was detected is described hereinabove with reference to Figs. 2–8.

[8691] VGAM624 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM624 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8692] VGAM624 gene, herein designated VGAM GENE, encodes a VGAM624 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM624 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM624 precursor RNA is designated SEQ ID:15972, and is provided hereinbelow with reference to the sequence listing part.

[8693] VGAM624 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM624 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8694] An enzyme complex designated DICER COMPLEX, dices the VGAM624 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM624 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM624 RNA is designated SEQ ID:15973, and

is provided hereinbelow with reference to the sequence listing part.

[8695] VGAM624 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM624 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM624 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8696] VGAM624 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM624 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM624 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM624 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM624 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8697] The complementary binding of VGAM624 RNA, herein designated VGAM RNA, to host target binding sites on VGAM624 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM624 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM624 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8698] It is appreciated that VGAM624 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM624 host target genes. The mRNA of each one of this plurality of VGAM624 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM624 RNA, herein designated VGAM RNA, and which when bound by VGAM624 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM624 host target proteins.

[8699] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM624 gene, herein designated VGAM GENE, on one or more VGAM624 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).



[8700] It is yet further appreciated that a function of VGAM624 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM624 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM624 correlate with, and may be deduced from, the identity of the host target genes which VGAM624 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8701] Nucleotide sequences of the VGAM624 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM624 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM624 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM624 are further described hereinbelow with reference to Table 1.

[8702] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM624 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8703] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 625 (VGAM625) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8704] VGAM625 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM625 was detected is described hereinabove with reference to Figs. 2–8.

[8705] VGAM625 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 41. VGAM625 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8706] VGAM625 gene, herein designated VGAM GENE, encodes a VGAM625 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM625 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM625 precursor RNA is

designated SEQ ID:15988, and is provided hereinbelow with reference to the sequence listing part.

[8707] VGAM625 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM625 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8708] An enzyme complex designated DICER COMPLEX, dices the VGAM625 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM625 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM625 RNA is designated SEQ ID:15989, and is provided hereinbelow with reference to the sequence

listing part.

[8709] VGAM625 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM625 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM625 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8710] VGAM625 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM625 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM625 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM625 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM625 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8711] The complementary binding of VGAM625 RNA, herein designated VGAM RNA, to host target binding sites on VGAM625 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM625 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM625 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8712] It is appreciated that VGAM625 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM625 host target genes. The mRNA of each one of this plurality of VGAM625 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM625 RNA, herein designated VGAM RNA, and which when bound by VGAM625 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM625 host target proteins.

[8713] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM625 gene, herein designated VGAM GENE, on one or more VGAM625 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8714] It is yet further appreciated that a function of VGAM625 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM625 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 41. Specific functions, and accordingly utilities, of VGAM625 correlate with, and may be deduced from, the identity of the host target genes which VGAM625 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8715] Nucleotide sequences of the VGAM625 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM625 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM625 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM625 are further described hereinbelow with reference to Table 1.

[8716] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM625 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8717] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 626 (VGAM626) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8718] VGAM626 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM626 was detected is described hereinabove with reference to Figs. 2–8.

[8719] VGAM626 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM626 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8720] VGAM626 gene, herein designated VGAM GENE, encodes a VGAM626 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM626 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM626 precursor RNA is designated SEQ ID:16009, and is provided hereinbelow



with reference to the sequence listing part.

[8721] VGAM626 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM626 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8722] An enzyme complex designated DICER COMPLEX, dices the VGAM626 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM626 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM626 RNA is designated SEQ ID:16010, and is provided hereinbelow with reference to the sequence listing part.

[8723] VGAM626 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM626 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM626 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8724] VGAM626 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM626 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM626 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM626 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM626 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8725] The complementary binding of VGAM626 RNA, herein designated VGAM RNA, to host target binding sites on VGAM626 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM626 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM626 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8726] It is appreciated that VGAM626 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM626 host target genes. The mRNA of each one of this plurality of VGAM626 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM626 RNA, herein designated VGAM RNA, and which when bound by VGAM626 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM626 host target proteins.

[8727] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM626 gene, herein designated VGAM GENE, on one or more VGAM626 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8728] It is yet further appreciated that a function of VGAM626 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM626 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM626 correlate with, and may be deduced from, the identity of the host target genes which VGAM626 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8729] Nucleotide sequences of the VGAM626 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM626 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM626 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM626 are further described hereinbelow with reference to Table 1.

[8730] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM626 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8731] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 627 (VGAM627) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8732] VGAM627 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM627 was detected is described hereinabove with reference to Figs. 2–8.

[8733] VGAM627 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM627 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8734] VGAM627 gene, herein designated VGAM GENE, encodes a VGAM627 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM627 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM627 precursor RNA is designated SEQ ID:16029, and is provided hereinbelow with reference to the sequence listing part.

[8735] VGAM627 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM627 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8736] An enzyme complex designated DICER COMPLEX, dices the VGAM627 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM627 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM627 RNA is designated SEQ ID:16030, and is provided hereinbelow with reference to the sequence listing part.

[8737] VGAM627 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM627 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM627 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8738] VGAM627 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM627 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM627 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM627 RNA, herein designated VGAM RNA, may have a different number of host target



binding sites in untranslated regions of a VGAM627 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8739] The complementary binding of VGAM627 RNA, herein designated VGAM RNA, to host target binding sites on VGAM627 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM627 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM627 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8740] It is appreciated that VGAM627 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM627 host target genes. The mRNA of each one of this plurality of VGAM627 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM627 RNA, herein designated VGAM

RNA, and which when bound by VGAM627 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM627 host target proteins.

[8741] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM627 gene, herein designated VGAM GENE, on one or more VGAM627 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8742] It is yet further appreciated that a function of VGAM627 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM627 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM627 correlate with, and may be deduced from, the identity of the host target genes which VGAM627 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8743] Nucleotide sequences of the VGAM627 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM627 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM627 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM627 are further described hereinbelow with reference to Table 1.

[8744] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM627 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8745] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 628 (VGAM628) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8746] VGAM628 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM628 was detected is described hereinabove with reference to Figs. 2-8.

[8747] VGAM628 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 41. VGAM628 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8748] VGAM628 gene, herein designated VGAM GENE, encodes a VGAM628 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM628 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM628 precursor RNA is designated SEQ ID:16036, and is provided hereinbelow with reference to the sequence listing part.

[8749] VGAM628 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM628 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8750] An enzyme complex designated DICER COMPLEX, dices the VGAM628 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM628 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM628 RNA is designated SEQ ID:16037, and is provided hereinbelow with reference to the sequence listing part.

[8751] VGAM628 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM628 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM628 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8752] VGAM628 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM628 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM628 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM628 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM628 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8753] The complementary binding of VGAM628 RNA, herein designated VGAM RNA, to host target binding sites on VGAM628 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM628 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM628 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8754] It is appreciated that VGAM628 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM628 host target genes. The mRNA of each one of this plurality of VGAM628 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM628 RNA, herein designated VGAM RNA, and which when bound by VGAM628 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM628 host target proteins.

[8755] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM628 gene, herein designated VGAM GENE, on one or more VGAM628 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8756] It is yet further appreciated that a function of VGAM628 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM628 include diagnosis, prevention and



treatment of viral infection by Human papillomavirus type 41. Specific functions, and accordingly utilities, of VGAM628 correlate with, and may be deduced from, the identity of the host target genes which VGAM628 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8757] Nucleotide sequences of the VGAM628 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM628 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM628 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM628 are further described hereinbelow with reference to Table 1.

[8758] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM628 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8759] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 629 (VGAM629) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8760] VGAM629 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM629 was detected is described hereinabove with reference to Figs. 2–8.

[8761] VGAM629 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM629 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8762] VGAM629 gene, herein designated VGAM GENE, encodes a VGAM629 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM629 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM629 precursor RNA is designated SEQ ID:16054, and is provided hereinbelow with reference to the sequence listing part.

[8763] VGAM629 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM629 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8764] An enzyme complex designated DICER COMPLEX, dices the VGAM629 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM629 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM629 RNA is designated SEQ ID:16055, and is provided hereinbelow with reference to the sequence listing part.

[8765] VGAM629 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM629 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM629 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8766] VGAM629 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM629 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM629 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM629 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM629 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8767] The complementary binding of VGAM629 RNA, herein designated VGAM RNA, to host target binding sites on VGAM629 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM629 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM629 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8768] It is appreciated that VGAM629 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM629 host target genes. The mRNA of each one of this plurality of VGAM629 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM629 RNA, herein designated VGAM RNA, and which when bound by VGAM629 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM629 host target proteins.

[8769] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM629 gene, herein designated VGAM GENE, on one or more VGAM629 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8770] It is yet further appreciated that a function of VGAM629 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM629 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Spe-

cific functions, and accordingly utilities, of VGAM629 correlate with, and may be deduced from, the identity of the host target genes which VGAM629 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8771] Nucleotide sequences of the VGAM629 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM629 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM629 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM629 are further described hereinbelow with reference to Table 1.

[8772] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM629 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8773] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 630 (VGAM630) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[8774] VGAM630 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM630 was detected is described hereinabove with reference to Figs. 2–8.

[8775] VGAM630 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM630 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8776] VGAM630 gene, herein designated VGAM GENE, encodes a VGAM630 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM630 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM630 precursor RNA is designated SEQ ID:16064, and is provided hereinbelow with reference to the sequence listing part.

[8777] VGAM630 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM630 folded precursor RNA, herein designated VGAM FOLDED PRECUR-



SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8778] An enzyme complex designated DICER COMPLEX, dices the VGAM630 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM630 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM630 RNA is designated SEQ ID:16065, and is provided hereinbelow with reference to the sequence listing part.

[8779] VGAM630 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM630 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM630 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8780] VGAM630 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM630 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM630 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM630 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM630 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8781] The complementary binding of VGAM630 RNA, herein designated VGAM RNA, to host target binding sites on VGAM630 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM630 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM630 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8782] It is appreciated that VGAM630 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM630 host target genes. The mRNA of each one of this plurality of VGAM630 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM630 RNA, herein designated VGAM RNA, and which when bound by VGAM630 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM630 host target proteins.

[8783] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM630 gene, herein designated VGAM GENE, on one or more VGAM630 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8784] It is yet further appreciated that a function of VGAM630 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM630 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM630 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM630 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8785] Nucleotide sequences of the VGAM630 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM630 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM630 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM630 are further described hereinbelow with reference to Table 1.

[8786] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM630 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8787] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 631 (VGAM631) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[8788] VGAM631 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM631 was detected is described hereinabove with reference to Figs. 2–8.

[8789] VGAM631 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM631 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8790] VGAM631 gene, herein designated VGAM GENE, encodes a VGAM631 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM631 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM631 precursor RNA is designated SEQ ID:16152, and is provided hereinbelow with reference to the sequence listing part.

[8791] VGAM631 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM631 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8792] An enzyme complex designated DICER COMPLEX, dices the VGAM631 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM631 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM631 RNA is designated SEQ ID:16153, and is provided hereinbelow with reference to the sequence listing part.

[8793] VGAM631 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM631 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM631 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8794] VGAM631 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM631 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM631 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM631 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM631 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an



example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8795] The complementary binding of VGAM631 RNA, herein designated VGAM RNA, to host target binding sites on VGAM631 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM631 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM631 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8796] It is appreciated that VGAM631 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM631 host target genes. The mRNA of each one of this plurality of VGAM631 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM631 RNA, herein designated VGAM RNA, and which when bound by VGAM631 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM631 host target proteins.

[8797] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM631 gene, herein designated VGAM GENE, on one or more VGAM631 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8798] It is yet further appreciated that a function of VGAM631 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM631 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM631 correlate with, and may be deduced from, the identity of the

host target genes which VGAM631 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8799] Nucleotide sequences of the VGAM631 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM631 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM631 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM631 are further described hereinbelow with reference to Table 1.

[8800] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM631 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8801] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 632 (VGAM632) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8802] VGAM632 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM632 was detected is described hereinabove with reference to Figs. 2–8.

[8803] VGAM632 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM632 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8804] VGAM632 gene, herein designated VGAM GENE, encodes a VGAM632 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM632 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM632 precursor RNA is designated SEQ ID:16184, and is provided hereinbelow with reference to the sequence listing part.

[8805] VGAM632 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM632 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8806] An enzyme complex designated DICER COMPLEX, dices the VGAM632 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM632 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM632 RNA is designated SEQ ID:16185, and is provided hereinbelow with reference to the sequence listing part.

[8807] VGAM632 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM632 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM632 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8808] VGAM632 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM632 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM632 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM632 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM632 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8809] The complementary binding of VGAM632 RNA, herein designated VGAM RNA, to host target binding sites on VGAM632 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM632 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM632 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8810] It is appreciated that VGAM632 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM632 host target genes. The mRNA of each one of this plurality of VGAM632 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM632 RNA, herein designated VGAM RNA, and which when bound by VGAM632 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM632 host target proteins.

[8811] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM632 gene, herein designated VGAM GENE, on one or more VGAM632 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8812] It is yet further appreciated that a function of VGAM632 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM632 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM632 correlate with, and may be deduced from, the identity of the host target genes which VGAM632 binds and inhibits, and



the function of these host target genes, as elaborated hereinbelow.

[8813] Nucleotide sequences of the VGAM632 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM632 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM632 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM632 are further described hereinbelow with reference to Table 1.

[8814] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM632 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8815] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 633 (VGAM633) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8816] VGAM633 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM633 was detected is described hereinabove with reference to Figs. 2–8.

[8817] VGAM633 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM633 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8818] VGAM633 gene, herein designated VGAM GENE, encodes a VGAM633 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM633 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM633 precursor RNA is designated SEQ ID:16204, and is provided hereinbelow with reference to the sequence listing part.

[8819] VGAM633 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM633 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8820] An enzyme complex designated DICER COMPLEX, dices the VGAM633 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM633 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM633 RNA is designated SEQ ID:16205, and is provided hereinbelow with reference to the sequence listing part.

[8821] VGAM633 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM633 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM633 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8822] VGAM633 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM633 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM633 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM633 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM633 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[8823] The complementary binding of VGAM633 RNA, herein designated VGAM RNA, to host target binding sites on VGAM633 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM633 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM633 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8824] It is appreciated that VGAM633 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM633 host target genes. The mRNA of each one of this plurality of VGAM633 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM633 RNA, herein designated VGAM RNA, and which when bound by VGAM633 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM633 host target proteins.

[8825] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM633 gene, herein designated VGAM GENE, on one or more VGAM633 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8826] It is yet further appreciated that a function of VGAM633 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM633 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM633 correlate with, and may be deduced from, the identity of the host target genes which VGAM633 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[8827] Nucleotide sequences of the VGAM633 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM633 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM633 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM633 are further described hereinbelow with reference to Table 1.

[8828] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM633 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8829] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 634 (VGAM634) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8830] VGAM634 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM634 was detected is described hereinabove with reference to Figs. 2–8.

[8831] VGAM634 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM634 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8832] VGAM634 gene, herein designated VGAM GENE, encodes a VGAM634 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM634 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM634 precursor RNA is designated SEQ ID:16217, and is provided hereinbelow with reference to the sequence listing part.

[8833] VGAM634 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM634 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the



RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8834] An enzyme complex designated DICER COMPLEX, dices the VGAM634 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM634 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM634 RNA is designated SEQ ID:16218, and is provided hereinbelow with reference to the sequence listing part.

[8835] VGAM634 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM634 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM634 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[8836] VGAM634 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM634 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM634 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM634 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM634 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8837] The complementary binding of VGAM634 RNA, herein designated VGAM RNA, to host target binding sites on VGAM634 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM634 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM634 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8838] It is appreciated that VGAM634 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM634 host target genes. The mRNA of each one of this plurality of VGAM634 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM634 RNA, herein designated VGAM RNA, and which when bound by VGAM634 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM634 host target proteins.

[8839] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM634 gene, herein designated VGAM GENE, on one or

more VGAM634 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8840] It is yet further appreciated that a function of VGAM634 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM634 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM634 correlate with, and may be deduced from, the identity of the host target genes which VGAM634 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8841] Nucleotide sequences of the VGAM634 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM634 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM634 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM634 are further described hereinbelow with reference to Table 1.

[8842] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM634 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8843] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 635 (VGAM635) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8844] VGAM635 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM635 was detected is described

hereinabove with reference to Figs. 2–8.

[8845] VGAM635 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM635 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8846] VGAM635 gene, herein designated VGAM GENE, encodes a VGAM635 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM635 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM635 precursor RNA is designated SEQ ID:16229, and is provided hereinbelow with reference to the sequence listing part.

[8847] VGAM635 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM635 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8848] An enzyme complex designated DICER COMPLEX, dices the VGAM635 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM635 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM635 RNA is designated SEQ ID:16230, and is provided hereinbelow with reference to the sequence listing part.

[8849] VGAM635 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM635 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM635 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8850] VGAM635 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM635 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM635 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM635 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM635 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8851] The complementary binding of VGAM635 RNA, herein



designated VGAM RNA, to host target binding sites on VGAM635 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM635 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM635 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8852] It is appreciated that VGAM635 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM635 host target genes. The mRNA of each one of this plurality of VGAM635 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM635 RNA, herein designated VGAM RNA, and which when bound by VGAM635 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM635 host target proteins.

[8853] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM635 gene, herein designated VGAM GENE, on one or more VGAM635 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8854] It is yet further appreciated that a function of VGAM635 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM635 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM635 correlate with, and may be deduced from, the identity of the host target genes which VGAM635 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8855] Nucleotide sequences of the VGAM635 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM635 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM635 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM635 are further described hereinbelow with reference to Table 1.

[8856] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM635 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8857] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 636 (VGAM636) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8858] VGAM636 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM636 was detected is described hereinabove with reference to Figs. 2-8.

[8859] VGAM636 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM636 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8860] VGAM636 gene, herein designated VGAM GENE, encodes a VGAM636 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM636 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM636 precursor RNA is designated SEQ ID:16241, and is provided hereinbelow with reference to the sequence listing part.

[8861] VGAM636 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM636 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[8862] An enzyme complex designated DICER COMPLEX, dices the VGAM636 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM636 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM636 RNA is designated SEQ ID:16242, and is provided hereinbelow with reference to the sequence listing part.

[8863] VGAM636 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM636 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM636 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8864] VGAM636 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM636 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM636 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM636 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM636 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8865] The complementary binding of VGAM636 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM636 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM636 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM636 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8866] It is appreciated that VGAM636 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM636 host target genes. The mRNA of each one of this plurality of VGAM636 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM636 RNA, herein designated VGAM RNA, and which when bound by VGAM636 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM636 host target proteins.

[8867] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM636 gene, herein designated VGAM GENE, on one or more VGAM636 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8868] It is yet further appreciated that a function of VGAM636 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM636 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM636 correlate with, and may be deduced from, the identity of the host target genes which VGAM636 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8869] Nucleotide sequences of the VGAM636 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



diced VGAM636 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM636 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM636 are further described hereinbelow with reference to Table 1.

[8870] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM636 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8871] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 637 (VGAM637) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8872] VGAM637 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM637 was detected is described hereinabove with reference to Figs. 2-8.

[8873] VGAM637 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Chimpanzee cytomegalovirus. VGAM637 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8874] VGAM637 gene, herein designated VGAM GENE, encodes a VGAM637 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM637 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM637 precursor RNA is designated SEQ ID:16365, and is provided hereinbelow with reference to the sequence listing part.

[8875] VGAM637 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM637 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8876] An enzyme complex designated DICER COMPLEX, dices the VGAM637 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM637 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM637 RNA is designated SEQ ID:16366, and is provided hereinbelow with reference to the sequence listing part.

[8877] VGAM637 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM637 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM637 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8878] VGAM637 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM637 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM637 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM637 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM637 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8879] The complementary binding of VGAM637 RNA, herein designated VGAM RNA, to host target binding sites on VGAM637 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM637 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM637 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8880] It is appreciated that VGAM637 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM637 host target genes. The mRNA of each one of this plurality of VGAM637 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM637 RNA, herein designated VGAM RNA, and which when bound by VGAM637 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM637 host target proteins.

[8881] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM637 gene, herein designated VGAM GENE, on one or more VGAM637 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8882] It is yet further appreciated that a function of VGAM637 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM637 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM637 correlate with, and may be deduced from, the identity of the host target genes which VGAM637 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8883] Nucleotide sequences of the VGAM637 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM637 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM637 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM637 are further described hereinbelow with reference to Table 1.

[8884] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM637 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8885] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 638 (VGAM638) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8886] VGAM638 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM638 was detected is described hereinabove with reference to Figs. 2-8.

[8887] VGAM638 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5.

VGAM638 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8888] VGAM638 gene, herein designated VGAM GENE, encodes a VGAM638 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM638 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM638 precursor RNA is designated SEQ ID:16559, and is provided hereinbelow with reference to the sequence listing part.

[8889] VGAM638 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM638 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8890] An enzyme complex designated DICER COMPLEX, dices



the VGAM638 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM638 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM638 RNA is designated SEQ ID:16560, and is provided hereinbelow with reference to the sequence listing part.

[8891] VGAM638 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM638 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM638 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8892] VGAM638 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM638 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM638 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM638 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM638 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8893] The complementary binding of VGAM638 RNA, herein designated VGAM RNA, to host target binding sites on VGAM638 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM638 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM638 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8894] It is appreciated that VGAM638 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM638 host target genes. The mRNA of each one of this plurality of VGAM638 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM638 RNA, herein designated VGAM RNA, and which when bound by VGAM638 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM638 host target proteins.

[8895] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM638 gene, herein designated VGAM GENE, on one or more VGAM638 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8896] It is yet further appreciated that a function of VGAM638 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM638 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM638 correlate with, and may be deduced from, the identity of the host target genes which VGAM638 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8897] Nucleotide sequences of the VGAM638 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM638 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM638 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM638 are further described hereinbelow with reference to Table 1.

[8898] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM638 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8899] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 639 (VGAM639) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8900] VGAM639 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM639 was detected is described hereinabove with reference to Figs. 2-8.

[8901] VGAM639 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM639 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[8902] VGAM639 gene, herein designated VGAM GENE, encodes a VGAM639 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM639 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM639 precursor RNA is designated SEQ ID:16562, and is provided hereinbelow with reference to the sequence listing part.

[8903] VGAM639 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM639 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8904] An enzyme complex designated DICER COMPLEX, dices the VGAM639 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM639 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM639 RNA is designated SEQ ID:16563, and is provided hereinbelow with reference to the sequence listing part.

[8905] VGAM639 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM639 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM639 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8906] VGAM639 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM639 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM639 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM639 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM639 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8907] The complementary binding of VGAM639 RNA, herein designated VGAM RNA, to host target binding sites on VGAM639 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM639 host tar-



get RNA, herein designated VGAM HOST TARGET RNA, into VGAM639 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8908] It is appreciated that VGAM639 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM639 host target genes. The mRNA of each one of this plurality of VGAM639 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM639 RNA, herein designated VGAM RNA, and which when bound by VGAM639 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM639 host target proteins.

[8909] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM639 gene, herein designated VGAM GENE, on one or more VGAM639 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8910] It is yet further appreciated that a function of VGAM639 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM639 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM639 correlate with, and may be deduced from, the identity of the host target genes which VGAM639 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8911] Nucleotide sequences of the VGAM639 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM639 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM639 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM639 are further described hereinbelow with reference to Table 1.

[8912] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM639 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8913] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 640 (VGAM640) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8914] VGAM640 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM640 was detected is described hereinabove with reference to Figs. 2-8.

[8915] VGAM640 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM640 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[8916] VGAM640 gene, herein designated VGAM GENE, encodes a VGAM640 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM640 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM640 precursor RNA is designated SEQ ID:16625, and is provided hereinbelow with reference to the sequence listing part.

[8917] VGAM640 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM640 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8918] An enzyme complex designated DICER COMPLEX, dices the VGAM640 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM640 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM640 RNA is designated SEQ ID:16626, and is provided hereinbelow with reference to the sequence listing part.

[8919] VGAM640 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM640 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM640 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8920] VGAM640 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM640 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM640 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM640 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM640 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8921] The complementary binding of VGAM640 RNA, herein designated VGAM RNA, to host target binding sites on VGAM640 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM640 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM640 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8922] It is appreciated that VGAM640 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM640 host target genes. The mRNA of each one of this plurality of VGAM640 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM640 RNA, herein designated VGAM RNA, and which when bound by VGAM640 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM640 host target proteins.

[8923] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM640 gene, herein designated VGAM GENE, on one or more VGAM640 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8924] It is yet further appreciated that a function of VGAM640 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM640 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM640 correlate with, and may be deduced from, the identity of the host target genes which VGAM640 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8925] Nucleotide sequences of the VGAM640 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM640 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM640 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM640 are further de-



scribed hereinbelow with reference to Table 1.

[8926] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM640 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8927] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 641 (VGAM641) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8928] VGAM641 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM641 was detected is described hereinabove with reference to Figs. 2-8.

[8929] VGAM641 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM641 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8930] VGAM641 gene, herein designated VGAM GENE, encodes a VGAM641 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM641 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM641 precursor RNA is designated SEQ ID:16651, and is provided hereinbelow with reference to the sequence listing part.

[8931] VGAM641 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM641 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8932] An enzyme complex designated DICER COMPLEX, dices the VGAM641 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM641 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM641 RNA is designated SEQ ID:16652, and is provided hereinbelow with reference to the sequence listing part.

[8933] VGAM641 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM641 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM641 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8934] VGAM641 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM641 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM641 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM641 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM641 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8935] The complementary binding of VGAM641 RNA, herein designated VGAM RNA, to host target binding sites on VGAM641 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM641 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM641 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8936] It is appreciated that VGAM641 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM641 host target genes. The mRNA of each one of this plurality of VGAM641 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM641 RNA, herein designated VGAM RNA, and which when bound by VGAM641 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM641 host target proteins.

[8937] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM641 gene, herein designated VGAM GENE, on one or more VGAM641 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8938] It is yet further appreciated that a function of VGAM641 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM641 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM641 correlate with, and may be deduced from, the identity of the host target genes which VGAM641 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8939] Nucleotide sequences of the VGAM641 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM641 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM641 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM641 are further described hereinbelow with reference to Table 1.

[8940] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM641 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8941] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 642 (VGAM642) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8942] VGAM642 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM642 was detected is described hereinabove with reference to Figs. 2-8.

[8943] VGAM642 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM642 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8944] VGAM642 gene, herein designated VGAM GENE, encodes a

VGAM642 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM642 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM642 precursor RNA is designated SEQ ID:16714, and is provided hereinbelow with reference to the sequence listing part.

[8945] VGAM642 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM642 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8946] An enzyme complex designated DICER COMPLEX, dices the VGAM642 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM642 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM642 RNA is designated SEQ ID:16715, and is provided hereinbelow with reference to the sequence listing part.

[8947] VGAM642 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM642 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM642 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8948] VGAM642 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM642 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM642 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM642 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM642 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8949] The complementary binding of VGAM642 RNA, herein designated VGAM RNA, to host target binding sites on VGAM642 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM642 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM642 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[8950] It is appreciated that VGAM642 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM642 host target genes. The mRNA of each one of this plurality of VGAM642 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM642 RNA, herein designated VGAM RNA, and which when bound by VGAM642 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM642 host target proteins.

[8951] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM642 gene, herein designated VGAM GENE, on one or more VGAM642 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8952] It is yet further appreciated that a function of VGAM642 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM642 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM642 correlate with, and may be deduced from, the identity of the host target genes which VGAM642 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8953] Nucleotide sequences of the VGAM642 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM642 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM642 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM642 are further described hereinbelow with reference to Table 1.

[8954] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM642 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8955] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 643 (VGAM643) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8956] VGAM643 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM643 was detected is described hereinabove with reference to Figs. 2-8.

[8957] VGAM643 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM643 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8958] VGAM643 gene, herein designated VGAM GENE, encodes a VGAM643 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM643 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM643 precursor RNA is designated SEQ ID:16720, and is provided hereinbelow with reference to the sequence listing part.

[8959] VGAM643 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM643 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8960] An enzyme complex designated DICER COMPLEX, dices the VGAM643 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM643 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM643 RNA is designated SEQ ID:16721, and is provided hereinbelow with reference to the sequence listing part.

[8961] VGAM643 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM643 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM643 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8962] VGAM643 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM643 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM643 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM643 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM643 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8963] The complementary binding of VGAM643 RNA, herein designated VGAM RNA, to host target binding sites on VGAM643 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM643 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM643 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[8964] It is appreciated that VGAM643 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM643 host target genes. The mRNA of each one of this plurality of VGAM643 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM643 RNA, herein designated VGAM RNA, and which when bound by VGAM643 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM643 host target proteins.

[8965] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM643 gene, herein designated VGAM GENE, on one or more VGAM643 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8966] It is yet further appreciated that a function of VGAM643 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM643 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM643 correlate with, and may be deduced from, the identity of the host target genes which VGAM643 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8967] Nucleotide sequences of the VGAM643 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM643 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM643 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM643 are further described hereinbelow with reference to Table 1.

[8968] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM643 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8969] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 644 (VGAM644) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8970] VGAM644 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM644 was detected is described hereinabove with reference to Figs. 2–8.

[8971] VGAM644 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM644 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8972] VGAM644 gene, herein designated VGAM GENE, encodes a VGAM644 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM644 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM644 precursor RNA is designated SEQ ID:16723, and is provided hereinbelow with reference to the sequence listing part.

[8973] VGAM644 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM644 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8974] An enzyme complex designated DICER COMPLEX, dices the VGAM644 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM644 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM644 RNA is designated SEQ ID:16724, and is provided hereinbelow with reference to the sequence listing part.

[8975] VGAM644 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM644 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM644 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8976] VGAM644 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM644 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM644 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM644 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM644 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8977] The complementary binding of VGAM644 RNA, herein designated VGAM RNA, to host target binding sites on VGAM644 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM644 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM644 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8978] It is appreciated that VGAM644 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM644 host target genes. The mRNA of each one of this plurality of VGAM644 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM644 RNA, herein designated VGAM RNA, and which when bound by VGAM644 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM644 host target proteins.

[8979] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM644 gene, herein designated VGAM GENE, on one or more VGAM644 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[8980] It is yet further appreciated that a function of VGAM644 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM644 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM644 correlate with, and may be deduced from, the identity of the host target genes which VGAM644 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8981] Nucleotide sequences of the VGAM644 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM644 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM644 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM644 are further described hereinbelow with reference to Table 1.

[8982] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the



complementarity of each of these host target binding sites to VGAM644 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8983] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 645 (VGAM645) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8984] VGAM645 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM645 was detected is described hereinabove with reference to Figs. 2–8.

[8985] VGAM645 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM645 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8986] VGAM645 gene, herein designated VGAM GENE, encodes a VGAM645 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM645 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM645 precursor RNA is designated SEQ ID:16747, and is provided hereinbelow with reference to the sequence listing part.

[8987] VGAM645 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM645 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8988] An enzyme complex designated DICER COMPLEX, dices the VGAM645 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM645 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM645 RNA is designated SEQ ID:16748, and is provided hereinbelow with reference to the sequence listing part.

[8989] VGAM645 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM645 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM645 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[8990] VGAM645 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM645 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM645 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM645 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM645 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[8991] The complementary binding of VGAM645 RNA, herein designated VGAM RNA, to host target binding sites on VGAM645 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM645 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM645 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8992] It is appreciated that VGAM645 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM645 host target genes. The mRNA of each one of this plurality of VGAM645 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM645 RNA, herein designated VGAM RNA, and which when bound by VGAM645 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM645 host target proteins.

[8993] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM645 gene, herein designated VGAM GENE, on one or more VGAM645 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[8994] It is yet further appreciated that a function of VGAM645 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM645 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM645 correlate with, and may be deduced from, the identity of the host target genes which VGAM645 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8995] Nucleotide sequences of the VGAM645 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM645 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM645 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM645 are further described hereinbelow with reference to Table 1.

[8996] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM645 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8997] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 646 (VGAM646) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8998] VGAM646 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM646 was detected is described hereinabove with reference to Figs. 2–8.

[8999] VGAM646 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM646 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9000] VGAM646 gene, herein designated VGAM GENE, encodes a VGAM646 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM646 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM646 precursor RNA is designated SEQ ID:16750, and is provided hereinbelow with reference to the sequence listing part.

[9001] VGAM646 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM646 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9002] An enzyme complex designated DICER COMPLEX, dices the VGAM646 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM646 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-



quence of VGAM646 RNA is designated SEQ ID:16751, and is provided hereinbelow with reference to the sequence listing part.

[9003] VGAM646 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM646 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM646 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9004] VGAM646 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM646 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM646 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM646 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM646 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9005] The complementary binding of VGAM646 RNA, herein designated VGAM RNA, to host target binding sites on VGAM646 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM646 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM646 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9006] It is appreciated that VGAM646 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM646 host target genes. The mRNA of

each one of this plurality of VGAM646 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM646 RNA, herein designated VGAM RNA, and which when bound by VGAM646 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM646 host target proteins.

[9007] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM646 gene, herein designated VGAM GENE, on one or more VGAM646 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[9008] It is yet further appreciated that a function of VGAM646 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM646 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM646 correlate with, and may be deduced from, the identity of the host target genes which VGAM646 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9009] Nucleotide sequences of the VGAM646 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM646 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM646 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM646 are further described hereinbelow with reference to Table 1.

[9010] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM646 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[9011] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 647 (VGAM647) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9012] VGAM647 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM647 was detected is described hereinabove with reference to Figs. 2–8.

[9013] VGAM647 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM647 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9014] VGAM647 gene, herein designated VGAM GENE, encodes a VGAM647 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM647 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM647 precursor RNA is designated SEQ ID:16771, and is provided hereinbelow with reference to the sequence listing part.

[9015] VGAM647 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM647 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9016] An enzyme complex designated DICER COMPLEX, dices the VGAM647 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM647 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM647 RNA is designated SEQ ID:16772, and

is provided hereinbelow with reference to the sequence listing part.

[9017] VGAM647 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM647 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM647 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9018] VGAM647 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM647 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM647 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM647 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM647 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9019] The complementary binding of VGAM647 RNA, herein designated VGAM RNA, to host target binding sites on VGAM647 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM647 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM647 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9020] It is appreciated that VGAM647 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM647 host target genes. The mRNA of each one of this plurality of VGAM647 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM647 RNA, herein designated VGAM RNA, and which when bound by VGAM647 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM647 host target proteins.

[9021] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM647 gene, herein designated VGAM GENE, on one or more VGAM647 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9022] It is yet further appreciated that a function of VGAM647 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM647 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM647 correlate with, and may be deduced from, the identity of the host target genes which VGAM647 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9023] Nucleotide sequences of the VGAM647 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM647 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM647 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM647 are further described hereinbelow with reference to Table 1.

[9024] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM647 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9025] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 648 (VGAM648) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9026] VGAM648 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM648 was detected is described hereinabove with reference to Figs. 2–8.

[9027] VGAM648 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM648 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9028] VGAM648 gene, herein designated VGAM GENE, encodes a VGAM648 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM648 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM648 precursor RNA is

designated SEQ ID:16786, and is provided hereinbelow with reference to the sequence listing part.

[9029] VGAM648 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM648 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9030] An enzyme complex designated DICER COMPLEX, dices the VGAM648 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM648 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM648 RNA is designated SEQ ID:16787, and is provided hereinbelow with reference to the sequence

listing part.

[9031] VGAM648 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM648 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM648 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9032] VGAM648 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM648 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM648 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM648 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM648 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9033] The complementary binding of VGAM648 RNA, herein designated VGAM RNA, to host target binding sites on VGAM648 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM648 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM648 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9034] It is appreciated that VGAM648 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM648 host target genes. The mRNA of each one of this plurality of VGAM648 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM648 RNA, herein designated VGAM RNA, and which when bound by VGAM648 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM648 host target proteins.

[9035] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM648 gene, herein designated VGAM GENE, on one or more VGAM648 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9036] It is yet further appreciated that a function of VGAM648 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM648 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM648 correlate with, and may be deduced from, the identity of the host target genes which VGAM648 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9037] Nucleotide sequences of the VGAM648 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM648 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM648 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM648 are further described hereinbelow with reference to Table 1.

[9038] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM648 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9039] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 649 (VGAM649) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9040] VGAM649 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM649 was detected is described hereinabove with reference to Figs. 2–8.

[9041] VGAM649 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox virus. VGAM649 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9042] VGAM649 gene, herein designated VGAM GENE, encodes a VGAM649 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM649 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM649 precursor RNA is designated SEQ ID:16806, and is provided hereinbelow

with reference to the sequence listing part.

[9043] VGAM649 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM649 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9044] An enzyme complex designated DICER COMPLEX, dices the VGAM649 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM649 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM649 RNA is designated SEQ ID:16807, and is provided hereinbelow with reference to the sequence listing part.

[9045] VGAM649 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM649 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM649 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9046] VGAM649 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM649 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM649 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM649 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM649 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9047] The complementary binding of VGAM649 RNA, herein designated VGAM RNA, to host target binding sites on VGAM649 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM649 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM649 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9048] It is appreciated that VGAM649 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM649 host target genes. The mRNA of each one of this plurality of VGAM649 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM649 RNA, herein designated VGAM RNA, and which when bound by VGAM649 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM649 host target proteins.

[9049] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM649 gene, herein designated VGAM GENE, on one or more VGAM649 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9050] It is yet further appreciated that a function of VGAM649 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM649 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific functions, and accordingly utilities, of VGAM649 correlate with, and may be deduced from, the identity of the host target genes which VGAM649 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9051] Nucleotide sequences of the VGAM649 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM649 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM649 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM649 are further described hereinbelow with reference to Table 1.

[9052] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM649 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9053] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 650 (VGAM650) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9054] VGAM650 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM650 was detected is described hereinabove with reference to Figs. 2–8.

[9055] VGAM650 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM650 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9056] VGAM650 gene, herein designated VGAM GENE, encodes a VGAM650 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM650 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM650 precursor RNA is designated SEQ ID:16815, and is provided hereinbelow with reference to the sequence listing part.

[9057] VGAM650 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM650 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9058] An enzyme complex designated DICER COMPLEX, dices the VGAM650 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM650 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM650 RNA is designated SEQ ID:16816, and is provided hereinbelow with reference to the sequence listing part.

[9059] VGAM650 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM650 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM650 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9060] VGAM650 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM650 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM650 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM650 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM650 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9061] The complementary binding of VGAM650 RNA, herein designated VGAM RNA, to host target binding sites on VGAM650 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM650 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM650 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9062] It is appreciated that VGAM650 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM650 host target genes. The mRNA of each one of this plurality of VGAM650 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM650 RNA, herein designated VGAM RNA, and which when bound by VGAM650 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM650 host target proteins.

[9063] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM650 gene, herein designated VGAM GENE, on one or more VGAM650 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9064] It is yet further appreciated that a function of VGAM650 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM650 include diagnosis, prevention and

treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM650 correlate with, and may be deduced from, the identity of the host target genes which VGAM650 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9065] Nucleotide sequences of the VGAM650 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM650 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM650 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM650 are further described hereinbelow with reference to Table 1.

[9066] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM650 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9067] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 651 (VGAM651) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9068] VGAM651 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM651 was detected is described hereinabove with reference to Figs. 2–8.

[9069] VGAM651 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox virus.

VGAM651 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9070] VGAM651 gene, herein designated VGAM GENE, encodes a VGAM651 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM651 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM651 precursor RNA is designated SEQ ID:16831, and is provided hereinbelow with reference to the sequence listing part.

[9071] VGAM651 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM651 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9072] An enzyme complex designated DICER COMPLEX, dices the VGAM651 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM651 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM651 RNA is designated SEQ ID:16832, and is provided hereinbelow with reference to the sequence listing part.

[9073] VGAM651 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM651 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM651 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9074] VGAM651 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM651 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM651 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM651 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM651 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9075] The complementary binding of VGAM651 RNA, herein designated VGAM RNA, to host target binding sites on VGAM651 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM651 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM651 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9076] It is appreciated that VGAM651 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM651 host target genes. The mRNA of each one of this plurality of VGAM651 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM651 RNA, herein designated VGAM RNA, and which when bound by VGAM651 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM651 host target proteins.

[9077] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM651 gene, herein designated VGAM GENE, on one or more VGAM651 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9078] It is yet further appreciated that a function of VGAM651 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM651 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific

functions, and accordingly utilities, of VGAM651 correlate with, and may be deduced from, the identity of the host target genes which VGAM651 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9079] Nucleotide sequences of the VGAM651 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM651 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM651 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM651 are further described hereinbelow with reference to Table 1.

[9080] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM651 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9081] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 652 (VGAM652) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[9082] VGAM652 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM652 was detected is described hereinabove with reference to Figs. 2–8.

[9083] VGAM652 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM652 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9084] VGAM652 gene, herein designated VGAM GENE, encodes a VGAM652 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM652 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM652 precursor RNA is designated SEQ ID:16841, and is provided hereinbelow with reference to the sequence listing part.

[9085] VGAM652 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM652 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9086] An enzyme complex designated DICER COMPLEX, dices the VGAM652 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM652 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM652 RNA is designated SEQ ID:16842, and is provided hereinbelow with reference to the sequence listing part.

[9087] VGAM652 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM652 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM652 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9088] VGAM652 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM652 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM652 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM652 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM652 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9089] The complementary binding of VGAM652 RNA, herein designated VGAM RNA, to host target binding sites on VGAM652 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM652 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM652 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9090] It is appreciated that VGAM652 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM652 host target genes. The mRNA of each one of this plurality of VGAM652 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM652 RNA, herein designated VGAM RNA, and which when bound by VGAM652 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM652 host target proteins.

[9091] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM652 gene, herein designated VGAM GENE, on one or more VGAM652 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9092] It is yet further appreciated that a function of VGAM652 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM652 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM652 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM652 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9093] Nucleotide sequences of the VGAM652 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM652 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM652 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM652 are further described hereinbelow with reference to Table 1.

[9094] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM652 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9095] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 653 (VGAM653) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[9096] VGAM653 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM653 was detected is described hereinabove with reference to Figs. 2–8.

[9097] VGAM653 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM653 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9098] VGAM653 gene, herein designated VGAM GENE, encodes a VGAM653 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM653 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM653 precursor RNA is designated SEQ ID:16851, and is provided hereinbelow with reference to the sequence listing part.

[9099] VGAM653 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM653 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9100] An enzyme complex designated DICER COMPLEX, dices the VGAM653 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM653 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM653 RNA is designated SEQ ID:16852, and is provided hereinbelow with reference to the sequence listing part.

[9101] VGAM653 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM653 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM653 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9102] VGAM653 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM653 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM653 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM653 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM653 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9103] The complementary binding of VGAM653 RNA, herein designated VGAM RNA, to host target binding sites on VGAM653 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM653 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM653 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9104] It is appreciated that VGAM653 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM653 host target genes. The mRNA of each one of this plurality of VGAM653 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM653 RNA, herein designated VGAM RNA, and which when bound by VGAM653 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM653 host target proteins.

[9105] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM653 gene, herein designated VGAM GENE, on one or more VGAM653 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9106] It is yet further appreciated that a function of VGAM653 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM653 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM653 correlate with, and may be deduced from, the identity of the host target genes which VGAM653 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[9107] Nucleotide sequences of the VGAM653 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM653 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM653 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM653 are further described hereinbelow with reference to Table 1.

[9108] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM653 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9109] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 654 (VGAM654) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9110] VGAM654 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM654 was detected is described hereinabove with reference to Figs. 2–8.

[9111] VGAM654 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox virus.

VGAM654 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9112] VGAM654 gene, herein designated VGAM GENE, encodes a VGAM654 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM654 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM654 precursor RNA is designated SEQ ID:16856, and is provided hereinbelow with reference to the sequence listing part.

[9113] VGAM654 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM654 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9114] An enzyme complex designated DICER COMPLEX, dices the VGAM654 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM654 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM654 RNA is designated SEQ ID:16857, and is provided hereinbelow with reference to the sequence listing part.

[9115] VGAM654 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM654 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM654 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9116] VGAM654 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM654 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM654 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM654 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM654 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[9117] The complementary binding of VGAM654 RNA, herein designated VGAM RNA, to host target binding sites on VGAM654 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM654 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM654 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9118] It is appreciated that VGAM654 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM654 host target genes. The mRNA of each one of this plurality of VGAM654 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM654 RNA, herein designated VGAM RNA, and which when bound by VGAM654 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM654 host target proteins.

[9119] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM654 gene, herein designated VGAM GENE, on one or more VGAM654 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9120] It is yet further appreciated that a function of VGAM654 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM654 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific functions, and accordingly utilities, of VGAM654 correlate with, and may be deduced from, the identity of the host target genes which VGAM654 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[9121] Nucleotide sequences of the VGAM654 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM654 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM654 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM654 are further described hereinbelow with reference to Table 1.

[9122] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM654 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9123] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 655 (VGAM655) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9124] VGAM655 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM655 was detected is described hereinabove with reference to Figs. 2–8.

[9125] VGAM655 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet yellows virus.

VGAM655 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9126] VGAM655 gene, herein designated VGAM GENE, encodes a VGAM655 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM655 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM655 precursor RNA is designated SEQ ID:16878, and is provided hereinbelow with reference to the sequence listing part.

[9127] VGAM655 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM655 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9128] An enzyme complex designated DICER COMPLEX, dices the VGAM655 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM655 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM655 RNA is designated SEQ ID:16879, and is provided hereinbelow with reference to the sequence listing part.

[9129] VGAM655 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM655 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM655 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[9130] VGAM655 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM655 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM655 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM655 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM655 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9131] The complementary binding of VGAM655 RNA, herein designated VGAM RNA, to host target binding sites on VGAM655 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM655 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM655 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9132] It is appreciated that VGAM655 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM655 host target genes. The mRNA of each one of this plurality of VGAM655 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM655 RNA, herein designated VGAM RNA, and which when bound by VGAM655 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM655 host target proteins.

[9133] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM655 gene, herein designated VGAM GENE, on one or



more VGAM655 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9134] It is yet further appreciated that a function of VGAM655 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM655 include diagnosis, prevention and treatment of viral infection by Beet yellows virus. Specific functions, and accordingly utilities, of VGAM655 correlate with, and may be deduced from, the identity of the host target genes which VGAM655 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9135] Nucleotide sequences of the VGAM655 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM655 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM655 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM655 are further described hereinbelow with reference to Table 1.

[9136] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM655 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9137] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 656 (VGAM656) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9138] VGAM656 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM656 was detected is described

hereinabove with reference to Figs. 2–8.

[9139] VGAM656 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet yellows virus.

VGAM656 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9140] VGAM656 gene, herein designated VGAM GENE, encodes a VGAM656 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM656 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM656 precursor RNA is designated SEQ ID:16881, and is provided hereinbelow with reference to the sequence listing part.

[9141] VGAM656 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM656 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9142] An enzyme complex designated DICER COMPLEX, dices the VGAM656 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM656 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM656 RNA is designated SEQ ID:16882, and is provided hereinbelow with reference to the sequence listing part.

[9143] VGAM656 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM656 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM656 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9144] VGAM656 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM656 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM656 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM656 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM656 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9145] The complementary binding of VGAM656 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM656 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM656 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM656 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9146] It is appreciated that VGAM656 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM656 host target genes. The mRNA of each one of this plurality of VGAM656 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM656 RNA, herein designated VGAM RNA, and which when bound by VGAM656 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM656 host target proteins.

[9147] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM656 gene, herein designated VGAM GENE, on one or more VGAM656 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9148] It is yet further appreciated that a function of VGAM656 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM656 include diagnosis, prevention and treatment of viral infection by Beet yellows virus. Specific functions, and accordingly utilities, of VGAM656 correlate with, and may be deduced from, the identity of the host target genes which VGAM656 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9149] Nucleotide sequences of the VGAM656 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM656 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM656 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM656 are further described hereinbelow with reference to Table 1.

[9150] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM656 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9151] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 657 (VGAM657) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9152] VGAM657 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM657 was detected is described hereinabove with reference to Figs. 2-8.



[9153] VGAM657 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like disease virus. VGAM657 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9154] VGAM657 gene, herein designated VGAM GENE, encodes a VGAM657 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM657 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM657 precursor RNA is designated SEQ ID:16906, and is provided hereinbelow with reference to the sequence listing part.

[9155] VGAM657 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM657 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[9156] An enzyme complex designated DICER COMPLEX, dices the VGAM657 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM657 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM657 RNA is designated SEQ ID:16907, and is provided hereinbelow with reference to the sequence listing part.

[9157] VGAM657 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM657 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM657 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9158] VGAM657 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM657 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM657 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM657 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM657 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9159] The complementary binding of VGAM657 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM657 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM657 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM657 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9160] It is appreciated that VGAM657 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM657 host target genes. The mRNA of each one of this plurality of VGAM657 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM657 RNA, herein designated VGAM RNA, and which when bound by VGAM657 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM657 host target proteins.

[9161] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM657 gene, herein designated VGAM GENE, on one or more VGAM657 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9162] It is yet further appreciated that a function of VGAM657 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM657 include diagnosis, prevention and treatment of viral infection by Yaba-like disease virus. Specific functions, and accordingly utilities, of VGAM657 correlate with, and may be deduced from, the identity of the host target genes which VGAM657 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9163] Nucleotide sequences of the VGAM657 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM657 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM657 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM657 are further described hereinbelow with reference to Table 1.

[9164] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM657 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9165] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 658 (VGAM658) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9166] VGAM658 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM658 was detected is described hereinabove with reference to Figs. 2-8.

[9167] VGAM658 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Beet yellows virus.  
VGAM658 host target gene, herein designated VGAM  
HOST TARGET GENE, is a human gene contained in the  
human genome.

[9168] VGAM658 gene, herein designated VGAM GENE, encodes a  
VGAM658 precursor RNA, herein designated VGAM PRE-  
CURSOR RNA. Similar to other miRNA genes, and unlike  
most ordinary genes, VGAM658 precursor RNA, herein  
designated VGAM PRECURSOR RNA, does not encode a  
protein. A nucleotide sequence identical or highly similar  
to the nucleotide sequence of VGAM658 precursor RNA is  
designated SEQ ID:16946, and is provided hereinbelow  
with reference to the sequence listing part.

[9169] VGAM658 precursor RNA, herein designated VGAM PRE-  
CURSOR RNA, folds onto itself, forming VGAM658 folded  
precursor RNA, herein designated VGAM FOLDED PRECUR-  
SOR RNA, which has a two-dimensional hairpin structure.  
As is well known in the art, this hairpin structure, is typi-  
cal of RNA encoded by miRNA genes, and is due to the  
fact that the nucleotide sequence of the first half of the  
RNA encoded by a miRNA gene is an accurate or partial  
inversed-reversed sequence of the nucleotide sequence of  
the second half thereof.

[9170] An enzyme complex designated DICER COMPLEX, dices the VGAM658 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM658 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM658 RNA is designated SEQ ID:16947, and is provided hereinbelow with reference to the sequence listing part.

[9171] VGAM658 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM658 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM658 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9172] VGAM658 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM658 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM658 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM658 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM658 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9173] The complementary binding of VGAM658 RNA, herein designated VGAM RNA, to host target binding sites on VGAM658 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM658 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM658 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9174] It is appreciated that VGAM658 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM658 host target genes. The mRNA of each one of this plurality of VGAM658 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM658 RNA, herein designated VGAM RNA, and which when bound by VGAM658 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM658 host target proteins.

[9175] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM658 gene, herein designated VGAM GENE, on one or more VGAM658 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9176] It is yet further appreciated that a function of VGAM658 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM658 include diagnosis, prevention and treatment of viral infection by Beet yellows virus. Specific functions, and accordingly utilities, of VGAM658 correlate with, and may be deduced from, the identity of the host target genes which VGAM658 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9177] Nucleotide sequences of the VGAM658 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM658 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM658 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM658 are further described hereinbelow with reference to Table 1.

[9178] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM658 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9179] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 659 (VGAM659) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9180] VGAM659 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM659 was detected is described hereinabove with reference to Figs. 2-8.

[9181] VGAM659 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like disease virus.

VGAM659 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9182] VGAM659 gene, herein designated VGAM GENE, encodes a VGAM659 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM659 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM659 precursor RNA is designated SEQ ID:16951, and is provided hereinbelow with reference to the sequence listing part.

[9183] VGAM659 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM659 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9184] An enzyme complex designated DICER COMPLEX, dices

the VGAM659 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM659 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM659 RNA is designated SEQ ID:16952, and is provided hereinbelow with reference to the sequence listing part.

[9185] VGAM659 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM659 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM659 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9186] VGAM659 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM659 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM659 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM659 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM659 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9187] The complementary binding of VGAM659 RNA, herein designated VGAM RNA, to host target binding sites on VGAM659 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM659 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM659 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9188] It is appreciated that VGAM659 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM659 host target genes. The mRNA of each one of this plurality of VGAM659 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM659 RNA, herein designated VGAM RNA, and which when bound by VGAM659 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM659 host target proteins.

[9189] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM659 gene, herein designated VGAM GENE, on one or more VGAM659 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9190] It is yet further appreciated that a function of VGAM659 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM659 include diagnosis, prevention and treatment of viral infection by Yaba-like disease virus. Specific functions, and accordingly utilities, of VGAM659 correlate with, and may be deduced from, the identity of the host target genes which VGAM659 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9191] Nucleotide sequences of the VGAM659 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM659 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM659 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM659 are further described hereinbelow with reference to Table 1.

[9192] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM659 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9193] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 660 (VGAM660) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9194] VGAM660 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM660 was detected is described hereinabove with reference to Figs. 2–8.

[9195] VGAM660 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet yellows virus. VGAM660 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9196] VGAM660 gene, herein designated VGAM GENE, encodes a VGAM660 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM660 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM660 precursor RNA is

designated SEQ ID:16954, and is provided hereinbelow with reference to the sequence listing part.

[9197] VGAM660 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM660 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9198] An enzyme complex designated DICER COMPLEX, dices the VGAM660 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM660 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM660 RNA is designated SEQ ID:16955, and is provided hereinbelow with reference to the sequence

listing part.

[9199] VGAM660 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM660 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM660 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9200] VGAM660 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM660 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM660 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM660 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM660 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9201] The complementary binding of VGAM660 RNA, herein designated VGAM RNA, to host target binding sites on VGAM660 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM660 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM660 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9202] It is appreciated that VGAM660 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM660 host target genes. The mRNA of each one of this plurality of VGAM660 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM660 RNA, herein designated VGAM RNA, and which when bound by VGAM660 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM660 host target proteins.

[9203] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM660 gene, herein designated VGAM GENE, on one or more VGAM660 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9204] It is yet further appreciated that a function of VGAM660 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM660 include diagnosis, prevention and treatment of viral infection by Beet yellows virus. Specific functions, and accordingly utilities, of VGAM660 correlate with, and may be deduced from, the identity of the host target genes which VGAM660 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[9205] Nucleotide sequences of the VGAM660 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM660 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM660 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM660 are further described hereinbelow with reference to Table 1.

[9206] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM660 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9207] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 661 (VGAM661) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9208] VGAM661 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM661 was detected is described hereinabove with reference to Figs. 2–8.

[9209] VGAM661 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM661 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9210] VGAM661 gene, herein designated VGAM GENE, encodes a VGAM661 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM661 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM661 precursor RNA is designated SEQ ID:16978, and is provided hereinbelow

with reference to the sequence listing part.

[9211] VGAM661 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM661 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9212] An enzyme complex designated DICER COMPLEX, dices the VGAM661 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM661 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM661 RNA is designated SEQ ID:16979, and is provided hereinbelow with reference to the sequence listing part.

[9213] VGAM661 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM661 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM661 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9214] VGAM661 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM661 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM661 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM661 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM661 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9215] The complementary binding of VGAM661 RNA, herein designated VGAM RNA, to host target binding sites on VGAM661 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM661 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM661 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9216] It is appreciated that VGAM661 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM661 host target genes. The mRNA of each one of this plurality of VGAM661 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM661 RNA, herein designated VGAM RNA, and which when bound by VGAM661 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM661 host target proteins.

[9217] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM661 gene, herein designated VGAM GENE, on one or more VGAM661 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9218] It is yet further appreciated that a function of VGAM661 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM661 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM661 correlate with, and may be deduced from, the identity of the host target genes which VGAM661 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9219] Nucleotide sequences of the VGAM661 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM661 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM661 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM661 are further described hereinbelow with reference to Table 1.

[9220] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM661 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9221] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 662 (VGAM662) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9222] VGAM662 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM662 was detected is described hereinabove with reference to Figs. 2–8.

[9223] VGAM662 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM662 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9224] VGAM662 gene, herein designated VGAM GENE, encodes a VGAM662 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM662 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM662 precursor RNA is designated SEQ ID:16984, and is provided hereinbelow with reference to the sequence listing part.

[9225] VGAM662 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM662 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9226] An enzyme complex designated DICER COMPLEX, dices the VGAM662 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM662 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM662 RNA is designated SEQ ID:16985, and is provided hereinbelow with reference to the sequence listing part.

[9227] VGAM662 host target gene, herein designated VGAM



HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM662 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM662 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9228] VGAM662 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM662 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM662 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM662 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM662 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9229] The complementary binding of VGAM662 RNA, herein designated VGAM RNA, to host target binding sites on VGAM662 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM662 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM662 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9230] It is appreciated that VGAM662 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM662 host target genes. The mRNA of each one of this plurality of VGAM662 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM662 RNA, herein designated VGAM

RNA, and which when bound by VGAM662 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM662 host target proteins.

[9231] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM662 gene, herein designated VGAM GENE, on one or more VGAM662 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9232] It is yet further appreciated that a function of VGAM662 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM662 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM662 correlate with, and may be deduced from, the identity of the host target genes which VGAM662 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9233] Nucleotide sequences of the VGAM662 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM662 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM662 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM662 are further described hereinbelow with reference to Table 1.

[9234] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM662 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9235] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 663 (VGAM663) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9236] VGAM663 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM663 was detected is described hereinabove with reference to Figs. 2–8.

[9237] VGAM663 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM663 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9238] VGAM663 gene, herein designated VGAM GENE, encodes a VGAM663 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM663 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM663 precursor RNA is designated SEQ ID:16998, and is provided hereinbelow with reference to the sequence listing part.

[9239] VGAM663 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM663 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9240] An enzyme complex designated DICER COMPLEX, dices the VGAM663 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM663 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM663 RNA is designated SEQ ID:16999, and is provided hereinbelow with reference to the sequence listing part.

[9241] VGAM663 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM663 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM663 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9242] VGAM663 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM663 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM663 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM663 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM663 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9243] The complementary binding of VGAM663 RNA, herein designated VGAM RNA, to host target binding sites on VGAM663 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM663 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM663 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9244] It is appreciated that VGAM663 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM663 host target genes. The mRNA of each one of this plurality of VGAM663 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM663 RNA, herein designated VGAM RNA, and which when bound by VGAM663 RNA, herein



designated VGAM RNA, causes inhibition of translation of respective one or more VGAM663 host target proteins.

[9245] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM663 gene, herein designated VGAM GENE, on one or more VGAM663 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9246] It is yet further appreciated that a function of VGAM663 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM663 include diagnosis, prevention and

treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM663 correlate with, and may be deduced from, the identity of the host target genes which VGAM663 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9247] Nucleotide sequences of the VGAM663 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM663 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM663 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM663 are further described hereinbelow with reference to Table 1.

[9248] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM663 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9249] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 664 (VGAM664) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9250] VGAM664 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM664 was detected is described hereinabove with reference to Figs. 2–8.

[9251] VGAM664 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM664 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9252] VGAM664 gene, herein designated VGAM GENE, encodes a VGAM664 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM664 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM664 precursor RNA is designated SEQ ID:17008, and is provided hereinbelow with reference to the sequence listing part.

[9253] VGAM664 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM664 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9254] An enzyme complex designated DICER COMPLEX, dices the VGAM664 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM664 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM664 RNA is designated SEQ ID:17009, and is provided hereinbelow with reference to the sequence listing part.

[9255] VGAM664 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM664 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM664 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9256] VGAM664 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM664 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM664 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM664 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM664 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9257] The complementary binding of VGAM664 RNA, herein designated VGAM RNA, to host target binding sites on VGAM664 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM664 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM664 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9258] It is appreciated that VGAM664 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM664 host target genes. The mRNA of each one of this plurality of VGAM664 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM664 RNA, herein designated VGAM RNA, and which when bound by VGAM664 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM664 host target proteins.

[9259] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM664 gene, herein designated VGAM GENE, on one or more VGAM664 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9260] It is yet further appreciated that a function of VGAM664 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM664 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific

functions, and accordingly utilities, of VGAM664 correlate with, and may be deduced from, the identity of the host target genes which VGAM664 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9261] Nucleotide sequences of the VGAM664 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM664 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM664 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM664 are further described hereinbelow with reference to Table 1.

[9262] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM664 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9263] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 665 (VGAM665) viral gene, which modulates expression of respective host target genes thereof, the func-



tion and utility of which host target genes is known in the art.

[9264] VGAM665 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM665 was detected is described hereinabove with reference to Figs. 2–8.

[9265] VGAM665 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM665 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9266] VGAM665 gene, herein designated VGAM GENE, encodes a VGAM665 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM665 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM665 precursor RNA is designated SEQ ID:17034, and is provided hereinbelow with reference to the sequence listing part.

[9267] VGAM665 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM665 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9268] An enzyme complex designated DICER COMPLEX, dices the VGAM665 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM665 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM665 RNA is designated SEQ ID:17035, and is provided hereinbelow with reference to the sequence listing part.

[9269] VGAM665 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM665 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM665 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9270] VGAM665 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM665 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM665 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM665 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM665 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9271] The complementary binding of VGAM665 RNA, herein designated VGAM RNA, to host target binding sites on VGAM665 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM665 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM665 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9272] It is appreciated that VGAM665 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM665 host target genes. The mRNA of each one of this plurality of VGAM665 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM665 RNA, herein designated VGAM RNA, and which when bound by VGAM665 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM665 host target proteins.

[9273] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM665 gene, herein designated VGAM GENE, on one or more VGAM665 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9274] It is yet further appreciated that a function of VGAM665 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM665 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM665

correlate with, and may be deduced from, the identity of the host target genes which VGAM665 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9275] Nucleotide sequences of the VGAM665 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM665 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM665 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM665 are further described hereinbelow with reference to Table 1.

[9276] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM665 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9277] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 666 (VGAM666) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[9278] VGAM666 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM666 was detected is described hereinabove with reference to Figs. 2–8.

[9279] VGAM666 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM666 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9280] VGAM666 gene, herein designated VGAM GENE, encodes a VGAM666 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM666 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM666 precursor RNA is designated SEQ ID:17076, and is provided hereinbelow with reference to the sequence listing part.

[9281] VGAM666 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM666 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9282] An enzyme complex designated DICER COMPLEX, dices the VGAM666 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM666 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM666 RNA is designated SEQ ID:17077, and is provided hereinbelow with reference to the sequence listing part.

[9283] VGAM666 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM666 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM666 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-



gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9284] VGAM666 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM666 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM666 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM666 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM666 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9285] The complementary binding of VGAM666 RNA, herein designated VGAM RNA, to host target binding sites on VGAM666 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM666 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM666 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9286] It is appreciated that VGAM666 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM666 host target genes. The mRNA of each one of this plurality of VGAM666 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM666 RNA, herein designated VGAM RNA, and which when bound by VGAM666 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM666 host target proteins.

[9287] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM666 gene, herein designated VGAM GENE, on one or more VGAM666 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9288] It is yet further appreciated that a function of VGAM666 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM666 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM666 correlate with, and may be deduced from, the identity of

the host target genes which VGAM666 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9289] Nucleotide sequences of the VGAM666 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM666 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM666 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM666 are further described hereinbelow with reference to Table 1.

[9290] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM666 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9291] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 667 (VGAM667) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9292] VGAM667 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM667 was detected is described hereinabove with reference to Figs. 2–8.

[9293] VGAM667 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM667 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9294] VGAM667 gene, herein designated VGAM GENE, encodes a VGAM667 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM667 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM667 precursor RNA is designated SEQ ID:17099, and is provided hereinbelow with reference to the sequence listing part.

[9295] VGAM667 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM667 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9296] An enzyme complex designated DICER COMPLEX, dices the VGAM667 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM667 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM667 RNA is designated SEQ ID:17100, and is provided hereinbelow with reference to the sequence listing part.

[9297] VGAM667 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM667 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM667 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9298] VGAM667 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM667 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM667 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM667 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM667 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9299] The complementary binding of VGAM667 RNA, herein designated VGAM RNA, to host target binding sites on VGAM667 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM667 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM667 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9300] It is appreciated that VGAM667 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM667 host target genes. The mRNA of each one of this plurality of VGAM667 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM667 RNA, herein designated VGAM RNA, and which when bound by VGAM667 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM667 host target proteins.

[9301] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM667 gene, herein designated VGAM GENE, on one or more VGAM667 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9302] It is yet further appreciated that a function of VGAM667 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM667 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM667 correlate with, and may be deduced from, the identity of the host target genes which VGAM667 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[9303] Nucleotide sequences of the VGAM667 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM667 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM667 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM667 are further described hereinbelow with reference to Table 1.

[9304] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM667 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9305] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 668 (VGAM668) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9306] VGAM668 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM668 was detected is described hereinabove with reference to Figs. 2–8.

[9307] VGAM668 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM668 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9308] VGAM668 gene, herein designated VGAM GENE, encodes a VGAM668 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM668 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM668 precursor RNA is designated SEQ ID:17112, and is provided hereinbelow with reference to the sequence listing part.

[9309] VGAM668 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM668 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9310] An enzyme complex designated DICER COMPLEX, dices the VGAM668 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM668 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM668 RNA is designated SEQ ID:17113, and is provided hereinbelow with reference to the sequence listing part.

[9311] VGAM668 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM668 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM668 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9312] VGAM668 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM668 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM668 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM668 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM668 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[9313] The complementary binding of VGAM668 RNA, herein designated VGAM RNA, to host target binding sites on VGAM668 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM668 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM668 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9314] It is appreciated that VGAM668 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM668 host target genes. The mRNA of each one of this plurality of VGAM668 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM668 RNA, herein designated VGAM RNA, and which when bound by VGAM668 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM668 host target proteins.

[9315] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM668 gene, herein designated VGAM GENE, on one or more VGAM668 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9316] It is yet further appreciated that a function of VGAM668 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM668 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM668 correlate with, and may be deduced from, the identity of the host target genes which VGAM668 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[9317] Nucleotide sequences of the VGAM668 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM668 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM668 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM668 are further described hereinbelow with reference to Table 1.

[9318] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM668 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9319] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 669 (VGAM669) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9320] VGAM669 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The



method by which VGAM669 was detected is described hereinabove with reference to Figs. 2–8.

[9321] VGAM669 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7.

VGAM669 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9322] VGAM669 gene, herein designated VGAM GENE, encodes a VGAM669 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM669 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM669 precursor RNA is designated SEQ ID:17122, and is provided hereinbelow with reference to the sequence listing part.

[9323] VGAM669 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM669 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9324] An enzyme complex designated DICER COMPLEX, dices the VGAM669 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM669 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM669 RNA is designated SEQ ID:17123, and is provided hereinbelow with reference to the sequence listing part.

[9325] VGAM669 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM669 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM669 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[9326] VGAM669 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM669 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM669 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM669 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM669 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9327] The complementary binding of VGAM669 RNA, herein designated VGAM RNA, to host target binding sites on VGAM669 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM669 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM669 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9328] It is appreciated that VGAM669 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM669 host target genes. The mRNA of each one of this plurality of VGAM669 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM669 RNA, herein designated VGAM RNA, and which when bound by VGAM669 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM669 host target proteins.

[9329] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM669 gene, herein designated VGAM GENE, on one or

more VGAM669 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9330] It is yet further appreciated that a function of VGAM669 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM669 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM669 correlate with, and may be deduced from, the identity of the host target genes which VGAM669 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9331] Nucleotide sequences of the VGAM669 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM669 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM669 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM669 are further described hereinbelow with reference to Table 1.

[9332] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM669 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9333] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 670 (VGAM670) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9334] VGAM670 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM670 was detected is described

hereinabove with reference to Figs. 2–8.

[9335] VGAM670 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM670 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9336] VGAM670 gene, herein designated VGAM GENE, encodes a VGAM670 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM670 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM670 precursor RNA is designated SEQ ID:17131, and is provided hereinbelow with reference to the sequence listing part.

[9337] VGAM670 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM670 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9338] An enzyme complex designated DICER COMPLEX, dices the VGAM670 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM670 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM670 RNA is designated SEQ ID:17132, and is provided hereinbelow with reference to the sequence listing part.

[9339] VGAM670 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM670 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM670 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.



[9340] VGAM670 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM670 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM670 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM670 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM670 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9341] The complementary binding of VGAM670 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM670 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM670 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM670 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9342] It is appreciated that VGAM670 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM670 host target genes. The mRNA of each one of this plurality of VGAM670 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM670 RNA, herein designated VGAM RNA, and which when bound by VGAM670 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM670 host target proteins.

[9343] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM670 gene, herein designated VGAM GENE, on one or more VGAM670 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9344] It is yet further appreciated that a function of VGAM670 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM670 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM670 correlate with, and may be deduced from, the identity of the host target genes which VGAM670 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9345] Nucleotide sequences of the VGAM670 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM670 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM670 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM670 are further described hereinbelow with reference to Table 1.

[9346] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM670 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9347] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 671 (VGAM671) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9348] VGAM671 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM671 was detected is described hereinabove with reference to Figs. 2-8.

[9349] VGAM671 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM671 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9350] VGAM671 gene, herein designated VGAM GENE, encodes a VGAM671 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM671 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM671 precursor RNA is designated SEQ ID:17134, and is provided hereinbelow with reference to the sequence listing part.

[9351] VGAM671 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM671 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[9352] An enzyme complex designated DICER COMPLEX, dices the VGAM671 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM671 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM671 RNA is designated SEQ ID:17135, and is provided hereinbelow with reference to the sequence listing part.

[9353] VGAM671 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM671 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM671 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9354] VGAM671 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM671 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM671 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM671 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM671 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9355] The complementary binding of VGAM671 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM671 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM671 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM671 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9356] It is appreciated that VGAM671 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM671 host target genes. The mRNA of each one of this plurality of VGAM671 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM671 RNA, herein designated VGAM RNA, and which when bound by VGAM671 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM671 host target proteins.

[9357] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM671 gene, herein designated VGAM GENE, on one or more VGAM671 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9358] It is yet further appreciated that a function of VGAM671 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM671 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM671 correlate with, and may be deduced from, the identity of the host target genes which VGAM671 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9359] Nucleotide sequences of the VGAM671 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM671 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM671 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM671 are further described hereinbelow with reference to Table 1.

[9360] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM671 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9361] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 672 (VGAM672) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9362] VGAM672 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM672 was detected is described hereinabove with reference to Figs. 2-8.

[9363] VGAM672 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Lymphocystis disease virus 1. VGAM672 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9364] VGAM672 gene, herein designated VGAM GENE, encodes a VGAM672 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM672 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM672 precursor RNA is designated SEQ ID:17151, and is provided hereinbelow with reference to the sequence listing part.

[9365] VGAM672 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM672 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9366] An enzyme complex designated DICER COMPLEX, dices the VGAM672 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM672 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM672 RNA is designated SEQ ID:17152, and is provided hereinbelow with reference to the sequence listing part.

[9367] VGAM672 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM672 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM672 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9368] VGAM672 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM672 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM672 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM672 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM672 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9369] The complementary binding of VGAM672 RNA, herein designated VGAM RNA, to host target binding sites on VGAM672 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM672 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM672 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9370] It is appreciated that VGAM672 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM672 host target genes. The mRNA of each one of this plurality of VGAM672 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM672 RNA, herein designated VGAM RNA, and which when bound by VGAM672 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM672 host target proteins.

[9371] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM672 gene, herein designated VGAM GENE, on one or more VGAM672 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9372] It is yet further appreciated that a function of VGAM672 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM672 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM672 correlate with, and may be deduced from, the identity of the host target genes which VGAM672 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9373] Nucleotide sequences of the VGAM672 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM672 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM672 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM672 are further described hereinbelow with reference to Table 1.

[9374] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM672 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9375] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 673 (VGAM673) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9376] VGAM673 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM673 was detected is described hereinabove with reference to Figs. 2-8.

[9377] VGAM673 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B.



VGAM673 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9378] VGAM673 gene, herein designated VGAM GENE, encodes a VGAM673 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM673 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM673 precursor RNA is designated SEQ ID:17161, and is provided hereinbelow with reference to the sequence listing part.

[9379] VGAM673 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM673 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9380] An enzyme complex designated DICER COMPLEX, dices

the VGAM673 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM673 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM673 RNA is designated SEQ ID:17162, and is provided hereinbelow with reference to the sequence listing part.

[9381] VGAM673 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM673 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM673 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9382] VGAM673 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM673 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM673 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM673 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM673 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9383] The complementary binding of VGAM673 RNA, herein designated VGAM RNA, to host target binding sites on VGAM673 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM673 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM673 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9384] It is appreciated that VGAM673 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM673 host target genes. The mRNA of each one of this plurality of VGAM673 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM673 RNA, herein designated VGAM RNA, and which when bound by VGAM673 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM673 host target proteins.

[9385] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM673 gene, herein designated VGAM GENE, on one or more VGAM673 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9386] It is yet further appreciated that a function of VGAM673 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM673 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM673 correlate with, and may be deduced from, the identity of the host target genes which VGAM673 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9387] Nucleotide sequences of the VGAM673 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM673 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM673 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM673 are further described hereinbelow with reference to Table 1.

[9388] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM673 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9389] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 674 (VGAM674) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9390] VGAM674 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM674 was detected is described hereinabove with reference to Figs. 2-8.

[9391] VGAM674 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM674 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9392] VGAM674 gene, herein designated VGAM GENE, encodes a VGAM674 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM674 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM674 precursor RNA is designated SEQ ID:17170, and is provided hereinbelow with reference to the sequence listing part.

[9393] VGAM674 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM674 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9394] An enzyme complex designated DICER COMPLEX, dices the VGAM674 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM674 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM674 RNA is designated SEQ ID:17171, and is provided hereinbelow with reference to the sequence listing part.

[9395] VGAM674 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM674 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM674 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9396] VGAM674 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM674 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM674 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM674 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM674 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9397] The complementary binding of VGAM674 RNA, herein designated VGAM RNA, to host target binding sites on VGAM674 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM674 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM674 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9398] It is appreciated that VGAM674 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM674 host target genes. The mRNA of each one of this plurality of VGAM674 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM674 RNA, herein designated VGAM RNA, and which when bound by VGAM674 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM674 host target proteins.

[9399] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM674 gene, herein designated VGAM GENE, on one or more VGAM674 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9400] It is yet further appreciated that a function of VGAM674 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM674 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM674 correlate with, and may be deduced from, the identity of the host target genes which VGAM674 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9401] Nucleotide sequences of the VGAM674 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM674 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM674 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM674 are further described hereinbelow with reference to Table 1.

[9402] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM674 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9403] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 675 (VGAM675) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9404] VGAM675 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM675 was detected is described hereinabove with reference to Figs. 2-8.

[9405] VGAM675 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM675 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[9406] VGAM675 gene, herein designated VGAM GENE, encodes a VGAM675 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM675 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM675 precursor RNA is designated SEQ ID:17178, and is provided hereinbelow with reference to the sequence listing part.

[9407] VGAM675 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM675 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9408] An enzyme complex designated DICER COMPLEX, dices the VGAM675 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM675 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM675 RNA is designated SEQ ID:17179, and is provided hereinbelow with reference to the sequence listing part.

[9409] VGAM675 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM675 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM675 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9410] VGAM675 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM675 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM675 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM675 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM675 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9411] The complementary binding of VGAM675 RNA, herein designated VGAM RNA, to host target binding sites on VGAM675 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM675 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM675 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9412] It is appreciated that VGAM675 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM675 host target genes. The mRNA of each one of this plurality of VGAM675 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM675 RNA, herein designated VGAM RNA, and which when bound by VGAM675 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM675 host target proteins.

[9413] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM675 gene, herein designated VGAM GENE, on one or more VGAM675 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9414] It is yet further appreciated that a function of VGAM675 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM675 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM675 correlate with, and may be deduced from, the identity of the host target genes which VGAM675 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9415] Nucleotide sequences of the VGAM675 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM675 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM675 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM675 are further de-

scribed hereinbelow with reference to Table 1.

[9416] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM675 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9417] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 676 (VGAM676) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9418] VGAM676 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM676 was detected is described hereinabove with reference to Figs. 2-8.

[9419] VGAM676 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Galleria mellonella densovirus. VGAM676 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9420] VGAM676 gene, herein designated VGAM GENE, encodes a VGAM676 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM676 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM676 precursor RNA is designated SEQ ID:17195, and is provided hereinbelow with reference to the sequence listing part.

[9421] VGAM676 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM676 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9422] An enzyme complex designated DICER COMPLEX, dices the VGAM676 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM676 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM676 RNA is designated SEQ ID:17196, and is provided hereinbelow with reference to the sequence listing part.

[9423] VGAM676 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM676 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM676 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9424] VGAM676 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM676 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM676 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM676 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM676 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9425] The complementary binding of VGAM676 RNA, herein designated VGAM RNA, to host target binding sites on VGAM676 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM676 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM676 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9426] It is appreciated that VGAM676 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM676 host target genes. The mRNA of each one of this plurality of VGAM676 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM676 RNA, herein designated VGAM RNA, and which when bound by VGAM676 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM676 host target proteins.

[9427] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM676 gene, herein designated VGAM GENE, on one or more VGAM676 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9428] It is yet further appreciated that a function of VGAM676 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM676 include diagnosis, prevention and treatment of viral infection by *Galleria mellonella* densovirus. Specific functions, and accordingly utilities, of VGAM676 correlate with, and may be deduced from, the identity of the host target genes which VGAM676 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9429] Nucleotide sequences of the VGAM676 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM676 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM676 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM676 are further described hereinbelow with reference to Table 1.

[9430] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM676 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9431] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 677 (VGAM677) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9432] VGAM677 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM677 was detected is described hereinabove with reference to Figs. 2-8.

[9433] VGAM677 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV-1. VGAM677 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9434] VGAM677 gene, herein designated VGAM GENE, encodes a



VGAM677 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM677 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM677 precursor RNA is designated SEQ ID:17203, and is provided hereinbelow with reference to the sequence listing part.

[9435] VGAM677 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM677 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9436] An enzyme complex designated DICER COMPLEX, dices the VGAM677 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM677 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM677 RNA is designated SEQ ID:17204, and is provided hereinbelow with reference to the sequence listing part.

[9437] VGAM677 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM677 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM677 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9438] VGAM677 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM677 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM677 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM677 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM677 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9439] The complementary binding of VGAM677 RNA, herein designated VGAM RNA, to host target binding sites on VGAM677 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM677 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM677 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[9440] It is appreciated that VGAM677 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM677 host target genes. The mRNA of each one of this plurality of VGAM677 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM677 RNA, herein designated VGAM RNA, and which when bound by VGAM677 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM677 host target proteins.

[9441] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM677 gene, herein designated VGAM GENE, on one or more VGAM677 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9442] It is yet further appreciated that a function of VGAM677 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM677 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-1. Specific functions, and accordingly utilities, of VGAM677 correlate with, and may be deduced from, the identity of the host target genes which VGAM677 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9443] Nucleotide sequences of the VGAM677 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM677 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM677 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM677 are further described hereinbelow with reference to Table 1.

[9444] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM677 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9445] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 678 (VGAM678) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9446] VGAM678 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM678 was detected is described hereinabove with reference to Figs. 2-8.

[9447] VGAM678 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Galleria mellonella densovirus. VGAM678 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9448] VGAM678 gene, herein designated VGAM GENE, encodes a VGAM678 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM678 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM678 precursor RNA is designated SEQ ID:17230, and is provided hereinbelow with reference to the sequence listing part.

[9449] VGAM678 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM678 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9450] An enzyme complex designated DICER COMPLEX, dices the VGAM678 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM678 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM678 RNA is designated SEQ ID:17231, and is provided hereinbelow with reference to the sequence listing part.

[9451] VGAM678 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM678 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM678 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9452] VGAM678 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM678 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM678 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host



target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM678 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM678 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9453] The complementary binding of VGAM678 RNA, herein designated VGAM RNA, to host target binding sites on VGAM678 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM678 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM678 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9454] It is appreciated that VGAM678 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM678 host target genes. The mRNA of each one of this plurality of VGAM678 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM678 RNA, herein designated VGAM RNA, and which when bound by VGAM678 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM678 host target proteins.

[9455] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM678 gene, herein designated VGAM GENE, on one or more VGAM678 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9456] It is yet further appreciated that a function of VGAM678 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM678 include diagnosis, prevention and treatment of viral infection by *Galleria mellonella* densovirus. Specific functions, and accordingly utilities, of VGAM678 correlate with, and may be deduced from, the identity of the host target genes which VGAM678 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9457] Nucleotide sequences of the VGAM678 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM678 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM678 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM678 are further described hereinbelow with reference to Table 1.

[9458] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM678 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9459] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 679 (VGAM679) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9460] VGAM679 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM679 was detected is described hereinabove with reference to Figs. 2–8.

[9461] VGAM679 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Galleria mellonella densovirus. VGAM679 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9462] VGAM679 gene, herein designated VGAM GENE, encodes a VGAM679 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM679 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM679 precursor RNA is designated SEQ ID:17241, and is provided hereinbelow with reference to the sequence listing part.

[9463] VGAM679 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM679 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9464] An enzyme complex designated DICER COMPLEX, dices the VGAM679 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM679 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM679 RNA is designated SEQ ID:17242, and is provided hereinbelow with reference to the sequence listing part.

[9465] VGAM679 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM679 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM679 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9466] VGAM679 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM679 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM679 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM679 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM679 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9467] The complementary binding of VGAM679 RNA, herein designated VGAM RNA, to host target binding sites on VGAM679 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM679 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM679 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9468] It is appreciated that VGAM679 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM679 host target genes. The mRNA of each one of this plurality of VGAM679 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM679 RNA, herein designated VGAM RNA, and which when bound by VGAM679 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM679 host target proteins.

[9469] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM679 gene, herein designated VGAM GENE, on one or more VGAM679 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9470] It is yet further appreciated that a function of VGAM679 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM679 include diagnosis, prevention and treatment of viral infection by *Galleria mellonella* denso-virus. Specific functions, and accordingly utilities, of VGAM679 correlate with, and may be deduced from, the identity of the host target genes which VGAM679 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9471] Nucleotide sequences of the VGAM679 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM679 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM679 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM679 are further described hereinbelow with reference to Table 1.

[9472] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM679 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9473] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 680 (VGAM680) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9474] VGAM680 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM680 was detected is described hereinabove with reference to Figs. 2–8.

[9475] VGAM680 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM680 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9476] VGAM680 gene, herein designated VGAM GENE, encodes a VGAM680 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM680 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM680 precursor RNA is designated SEQ ID:17265, and is provided hereinbelow with reference to the sequence listing part.

[9477] VGAM680 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM680 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9478] An enzyme complex designated DICER COMPLEX, dices the VGAM680 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM680 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 55%) nucleotide sequence of VGAM680 RNA is designated SEQ ID:17266, and is provided hereinbelow with reference to the sequence listing part.

[9479] VGAM680 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM680 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM680 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9480] VGAM680 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM680 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM680 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM680 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM680 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9481] The complementary binding of VGAM680 RNA, herein designated VGAM RNA, to host target binding sites on VGAM680 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM680 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM680 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9482] It is appreciated that VGAM680 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM680 host target genes. The mRNA of each one of this plurality of VGAM680 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM680 RNA, herein designated VGAM RNA, and which when bound by VGAM680 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM680 host target proteins.

[9483] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM680 gene, herein designated VGAM GENE, on one or more VGAM680 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[9484] It is yet further appreciated that a function of VGAM680 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM680 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM680 correlate with, and may be deduced from, the identity of the host target genes which VGAM680 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9485] Nucleotide sequences of the VGAM680 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM680 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM680 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM680 are further described hereinbelow with reference to Table 1.

[9486] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM680 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9487] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 681 (VGAM681) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9488] VGAM681 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM681 was detected is described hereinabove with reference to Figs. 2–8.

[9489] VGAM681 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM681 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9490] VGAM681 gene, herein designated VGAM GENE, encodes a VGAM681 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM681 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a



protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM681 precursor RNA is designated SEQ ID:17283, and is provided hereinbelow with reference to the sequence listing part.

[9491] VGAM681 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM681 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9492] An enzyme complex designated DICER COMPLEX, dices the VGAM681 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM681 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM681 RNA is designated SEQ ID:17284, and is provided hereinbelow with reference to the sequence listing part.

[9493] VGAM681 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM681 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM681 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9494] VGAM681 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM681 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM681 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM681 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM681 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9495] The complementary binding of VGAM681 RNA, herein designated VGAM RNA, to host target binding sites on VGAM681 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM681 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM681 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9496] It is appreciated that VGAM681 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM681 host target genes. The mRNA of

each one of this plurality of VGAM681 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM681 RNA, herein designated VGAM RNA, and which when bound by VGAM681 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM681 host target proteins.

[9497] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM681 gene, herein designated VGAM GENE, on one or more VGAM681 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[9498] It is yet further appreciated that a function of VGAM681 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM681 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM681 correlate with, and may be deduced from, the identity of the host target genes which VGAM681 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9499] Nucleotide sequences of the VGAM681 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM681 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM681 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM681 are further described hereinbelow with reference to Table 1.

[9500] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM681 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[9501] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 682 (VGAM682) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9502] VGAM682 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM682 was detected is described hereinabove with reference to Figs. 2–8.

[9503] VGAM682 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM682 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9504] VGAM682 gene, herein designated VGAM GENE, encodes a VGAM682 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM682 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM682 precursor RNA is designated SEQ ID:17322, and is provided hereinbelow with reference to the sequence listing part.

[9505] VGAM682 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM682 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9506] An enzyme complex designated DICER COMPLEX, dices the VGAM682 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM682 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM682 RNA is designated SEQ ID:17323, and

is provided hereinbelow with reference to the sequence listing part.

[9507] VGAM682 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM682 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM682 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9508] VGAM682 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM682 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM682 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM682 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM682 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9509] The complementary binding of VGAM682 RNA, herein designated VGAM RNA, to host target binding sites on VGAM682 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM682 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM682 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9510] It is appreciated that VGAM682 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM682 host target genes. The mRNA of each one of this plurality of VGAM682 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM682 RNA, herein designated VGAM RNA, and which when bound by VGAM682 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM682 host target proteins.

[9511] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM682 gene, herein designated VGAM GENE, on one or more VGAM682 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9512] It is yet further appreciated that a function of VGAM682 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM682 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM682 correlate with, and may be deduced from, the identity of the host target genes which VGAM682 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9513] Nucleotide sequences of the VGAM682 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM682 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM682 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM682 are further described hereinbelow with reference to Table 1.

[9514] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM682 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9515] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 683 (VGAM683) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9516] VGAM683 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM683 was detected is described hereinabove with reference to Figs. 2–8.

[9517] VGAM683 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM683 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9518] VGAM683 gene, herein designated VGAM GENE, encodes a VGAM683 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM683 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM683 precursor RNA is

designated SEQ ID:17351, and is provided hereinbelow with reference to the sequence listing part.

[9519] VGAM683 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM683 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9520] An enzyme complex designated DICER COMPLEX, dices the VGAM683 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM683 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM683 RNA is designated SEQ ID:17352, and is provided hereinbelow with reference to the sequence

listing part.

[9521] VGAM683 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM683 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM683 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9522] VGAM683 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM683 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM683 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM683 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM683 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9523] The complementary binding of VGAM683 RNA, herein designated VGAM RNA, to host target binding sites on VGAM683 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM683 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM683 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9524] It is appreciated that VGAM683 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM683 host target genes. The mRNA of each one of this plurality of VGAM683 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM683 RNA, herein designated VGAM RNA, and which when bound by VGAM683 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM683 host target proteins.

[9525] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM683 gene, herein designated VGAM GENE, on one or more VGAM683 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9526] It is yet further appreciated that a function of VGAM683 is



inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM683 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM683 correlate with, and may be deduced from, the identity of the host target genes which VGAM683 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9527] Nucleotide sequences of the VGAM683 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM683 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM683 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM683 are further described hereinbelow with reference to Table 1.

[9528] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM683 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9529] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 684 (VGAM684) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9530] VGAM684 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM684 was detected is described hereinabove with reference to Figs. 2–8.

[9531] VGAM684 gene, herein designated VGAM GENE, is a viral gene contained in the genome of TT virus. VGAM684 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9532] VGAM684 gene, herein designated VGAM GENE, encodes a VGAM684 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM684 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM684 precursor RNA is designated SEQ ID:17362, and is provided hereinbelow with reference to the sequence listing part.

[9533] VGAM684 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM684 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9534] An enzyme complex designated DICER COMPLEX, dices the VGAM684 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM684 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM684 RNA is designated SEQ ID:17363, and is provided hereinbelow with reference to the sequence listing part.

[9535] VGAM684 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM684 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM684 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9536] VGAM684 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM684 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM684 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM684 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM684 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9537] The complementary binding of VGAM684 RNA, herein designated VGAM RNA, to host target binding sites on VGAM684 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM684 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM684 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9538] It is appreciated that VGAM684 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM684 host target genes. The mRNA of each one of this plurality of VGAM684 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM684 RNA, herein designated VGAM

RNA, and which when bound by VGAM684 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM684 host target proteins.

[9539] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM684 gene, herein designated VGAM GENE, on one or more VGAM684 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9540] It is yet further appreciated that a function of VGAM684 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM684 include diagnosis, prevention and treatment of viral infection by TT virus. Specific functions, and accordingly utilities, of VGAM684 correlate with, and may be deduced from, the identity of the host target genes which VGAM684 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9541] Nucleotide sequences of the VGAM684 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM684 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM684 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM684 are further described hereinbelow with reference to Table 1.

[9542] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM684 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9543] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 685 (VGAM685) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9544] VGAM685 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM685 was detected is described hereinabove with reference to Figs. 2–8.

[9545] VGAM685 gene, herein designated VGAM GENE, is a viral gene contained in the genome of TT virus. VGAM685 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9546] VGAM685 gene, herein designated VGAM GENE, encodes a VGAM685 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM685 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM685 precursor RNA is designated SEQ ID:17381, and is provided hereinbelow with reference to the sequence listing part.

[9547] VGAM685 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM685 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9548] An enzyme complex designated DICER COMPLEX, dices the VGAM685 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM685 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM685 RNA is designated SEQ ID:17382, and is provided hereinbelow with reference to the sequence listing part.

[9549] VGAM685 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM685 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM685 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9550] VGAM685 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM685 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM685 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM685 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM685 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9551] The complementary binding of VGAM685 RNA, herein designated VGAM RNA, to host target binding sites on VGAM685 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM685 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM685 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9552] It is appreciated that VGAM685 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM685 host target genes. The mRNA of each one of this plurality of VGAM685 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM685 RNA, herein designated VGAM RNA, and which when bound by VGAM685 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM685 host target proteins.

[9553] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM685 gene, herein designated VGAM GENE, on one or more VGAM685 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9554] It is yet further appreciated that a function of VGAM685 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM685 include diagnosis, prevention and treatment of viral infection by TT virus. Specific functions,

and accordingly utilities, of VGAM685 correlate with, and may be deduced from, the identity of the host target genes which VGAM685 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9555] Nucleotide sequences of the VGAM685 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM685 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM685 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM685 are further described hereinbelow with reference to Table 1.

[9556] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM685 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9557] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 686 (VGAM686) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[9558] VGAM686 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM686 was detected is described hereinabove with reference to Figs. 2–8.

[9559] VGAM686 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM686 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9560] VGAM686 gene, herein designated VGAM GENE, encodes a VGAM686 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM686 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM686 precursor RNA is designated SEQ ID:17386, and is provided hereinbelow with reference to the sequence listing part.

[9561] VGAM686 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM686 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9562] An enzyme complex designated DICER COMPLEX, dices the VGAM686 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM686 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM686 RNA is designated SEQ ID:17387, and is provided hereinbelow with reference to the sequence listing part.

[9563] VGAM686 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM686 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM686 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9564] VGAM686 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM686 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM686 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM686 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM686 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9565] The complementary binding of VGAM686 RNA, herein designated VGAM RNA, to host target binding sites on VGAM686 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM686 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM686 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9566] It is appreciated that VGAM686 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM686 host target genes. The mRNA of each one of this plurality of VGAM686 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM686 RNA, herein designated VGAM RNA, and which when bound by VGAM686 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM686 host target proteins.

[9567] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM686 gene, herein designated VGAM GENE, on one or more VGAM686 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9568] It is yet further appreciated that a function of VGAM686 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM686 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM686 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM686 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9569] Nucleotide sequences of the VGAM686 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM686 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM686 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM686 are further described hereinbelow with reference to Table 1.

[9570] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM686 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9571] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 687 (VGAM687) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[9572] VGAM687 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM687 was detected is described hereinabove with reference to Figs. 2–8.

[9573] VGAM687 gene, herein designated VGAM GENE, is a viral gene contained in the genome of TT virus. VGAM687 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9574] VGAM687 gene, herein designated VGAM GENE, encodes a VGAM687 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM687 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM687 precursor RNA is designated SEQ ID:17395, and is provided hereinbelow with reference to the sequence listing part.

[9575] VGAM687 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM687 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9576] An enzyme complex designated DICER COMPLEX, dices the VGAM687 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM687 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM687 RNA is designated SEQ ID:17396, and is provided hereinbelow with reference to the sequence listing part.

[9577] VGAM687 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM687 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM687 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9578] VGAM687 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM687 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM687 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM687 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM687 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9579] The complementary binding of VGAM687 RNA, herein designated VGAM RNA, to host target binding sites on VGAM687 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM687 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM687 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9580] It is appreciated that VGAM687 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM687 host target genes. The mRNA of each one of this plurality of VGAM687 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM687 RNA, herein designated VGAM RNA, and which when bound by VGAM687 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM687 host target proteins.

[9581] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM687 gene, herein designated VGAM GENE, on one or more VGAM687 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9582] It is yet further appreciated that a function of VGAM687 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM687 include diagnosis, prevention and treatment of viral infection by TT virus. Specific functions, and accordingly utilities, of VGAM687 correlate with, and may be deduced from, the identity of the host target genes which VGAM687 binds and inhibits, and the func-



tion of these host target genes, as elaborated hereinbelow.

[9583] Nucleotide sequences of the VGAM687 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM687 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM687 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM687 are further described hereinbelow with reference to Table 1.

[9584] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM687 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9585] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 688 (VGAM688) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9586] VGAM688 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM688 was detected is described hereinabove with reference to Figs. 2–8.

[9587] VGAM688 gene, herein designated VGAM GENE, is a viral gene contained in the genome of TT virus. VGAM688 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9588] VGAM688 gene, herein designated VGAM GENE, encodes a VGAM688 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM688 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM688 precursor RNA is designated SEQ ID:17420, and is provided hereinbelow with reference to the sequence listing part.

[9589] VGAM688 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM688 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9590] An enzyme complex designated DICER COMPLEX, dices the VGAM688 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM688 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM688 RNA is designated SEQ ID:17421, and is provided hereinbelow with reference to the sequence listing part.

[9591] VGAM688 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM688 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM688 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[9592] VGAM688 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM688 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM688 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM688 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM688 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9593] The complementary binding of VGAM688 RNA, herein designated VGAM RNA, to host target binding sites on VGAM688 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM688 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM688 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9594] It is appreciated that VGAM688 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM688 host target genes. The mRNA of each one of this plurality of VGAM688 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM688 RNA, herein designated VGAM RNA, and which when bound by VGAM688 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM688 host target proteins.

[9595] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM688 gene, herein designated VGAM GENE, on one or

more VGAM688 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9596] It is yet further appreciated that a function of VGAM688 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM688 include diagnosis, prevention and treatment of viral infection by TT virus. Specific functions, and accordingly utilities, of VGAM688 correlate with, and may be deduced from, the identity of the host target genes which VGAM688 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9597] Nucleotide sequences of the VGAM688 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM688 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM688 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM688 are further described hereinbelow with reference to Table 1.

[9598] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM688 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9599] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 689 (VGAM689) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9600] VGAM689 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM689 was detected is described

hereinabove with reference to Figs. 2–8.

[9601] VGAM689 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM689 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9602] VGAM689 gene, herein designated VGAM GENE, encodes a VGAM689 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM689 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM689 precursor RNA is designated SEQ ID:17433, and is provided hereinbelow with reference to the sequence listing part.

[9603] VGAM689 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM689 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9604] An enzyme complex designated DICER COMPLEX, dices the VGAM689 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM689 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM689 RNA is designated SEQ ID:17434, and is provided hereinbelow with reference to the sequence listing part.

[9605] VGAM689 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM689 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM689 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9606] VGAM689 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM689 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM689 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM689 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM689 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9607] The complementary binding of VGAM689 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM689 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM689 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM689 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9608] It is appreciated that VGAM689 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM689 host target genes. The mRNA of each one of this plurality of VGAM689 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM689 RNA, herein designated VGAM RNA, and which when bound by VGAM689 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM689 host target proteins.

[9609] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM689 gene, herein designated VGAM GENE, on one or more VGAM689 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9610] It is yet further appreciated that a function of VGAM689 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM689 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM689 correlate with, and may be deduced from, the identity of the host target genes which VGAM689 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9611] Nucleotide sequences of the VGAM689 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM689 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM689 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM689 are further described hereinbelow with reference to Table 1.

[9612] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM689 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9613] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 690 (VGAM690) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9614] VGAM690 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM690 was detected is described hereinabove with reference to Figs. 2-8.

[9615] VGAM690 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV-1. VGAM690 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9616] VGAM690 gene, herein designated VGAM GENE, encodes a VGAM690 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM690 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM690 precursor RNA is designated SEQ ID:17463, and is provided hereinbelow with reference to the sequence listing part.

[9617] VGAM690 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM690 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[9618] An enzyme complex designated DICER COMPLEX, dices the VGAM690 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM690 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM690 RNA is designated SEQ ID:17464, and is provided hereinbelow with reference to the sequence listing part.

[9619] VGAM690 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM690 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM690 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9620] VGAM690 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM690 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM690 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM690 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM690 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9621] The complementary binding of VGAM690 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM690 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM690 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM690 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9622] It is appreciated that VGAM690 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM690 host target genes. The mRNA of each one of this plurality of VGAM690 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM690 RNA, herein designated VGAM RNA, and which when bound by VGAM690 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM690 host target proteins.

[9623] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM690 gene, herein designated VGAM GENE, on one or more VGAM690 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9624] It is yet further appreciated that a function of VGAM690 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM690 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-1. Specific functions, and accordingly utilities, of VGAM690 correlate with, and may be deduced from, the identity of the host target genes which VGAM690 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9625] Nucleotide sequences of the VGAM690 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM690 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM690 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM690 are further described hereinbelow with reference to Table 1.

[9626] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM690 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9627] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 691 (VGAM691) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9628] VGAM691 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM691 was detected is described hereinabove with reference to Figs. 2-8.

[9629] VGAM691 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Macaca mulatta* rhadinovirus. VGAM691 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9630] VGAM691 gene, herein designated VGAM GENE, encodes a VGAM691 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM691 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM691 precursor RNA is designated SEQ ID:17473, and is provided hereinbelow with reference to the sequence listing part.

[9631] VGAM691 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM691 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9632] An enzyme complex designated DICER COMPLEX, dices the VGAM691 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM691 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM691 RNA is designated SEQ ID:17474, and is provided hereinbelow with reference to the sequence listing part.

[9633] VGAM691 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM691 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM691 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9634] VGAM691 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM691 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM691 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM691 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM691 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9635] The complementary binding of VGAM691 RNA, herein designated VGAM RNA, to host target binding sites on VGAM691 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM691 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM691 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9636] It is appreciated that VGAM691 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM691 host target genes. The mRNA of each one of this plurality of VGAM691 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM691 RNA, herein designated VGAM RNA, and which when bound by VGAM691 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM691 host target proteins.

[9637] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM691 gene, herein designated VGAM GENE, on one or more VGAM691 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9638] It is yet further appreciated that a function of VGAM691 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM691 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM691 correlate with, and may be deduced from, the identity of the host target genes which VGAM691 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9639] Nucleotide sequences of the VGAM691 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM691 RNA, herein designated VGAM RNA, and a



schematic representation of the secondary folding of VGAM691 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM691 are further described hereinbelow with reference to Table 1.

[9640] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM691 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9641] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 692 (VGAM692) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9642] VGAM692 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM692 was detected is described hereinabove with reference to Figs. 2-8.

[9643] VGAM692 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Macaca mulatta rhadi-*

novirus. VGAM692 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9644] VGAM692 gene, herein designated VGAM GENE, encodes a VGAM692 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM692 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM692 precursor RNA is designated SEQ ID:17533, and is provided hereinbelow with reference to the sequence listing part.

[9645] VGAM692 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM692 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9646] An enzyme complex designated DICER COMPLEX, dices

the VGAM692 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM692 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM692 RNA is designated SEQ ID:17534, and is provided hereinbelow with reference to the sequence listing part.

[9647] VGAM692 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM692 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM692 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9648] VGAM692 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM692 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM692 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM692 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM692 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9649] The complementary binding of VGAM692 RNA, herein designated VGAM RNA, to host target binding sites on VGAM692 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM692 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM692 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9650] It is appreciated that VGAM692 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM692 host target genes. The mRNA of each one of this plurality of VGAM692 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM692 RNA, herein designated VGAM RNA, and which when bound by VGAM692 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM692 host target proteins.

[9651] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM692 gene, herein designated VGAM GENE, on one or more VGAM692 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9652] It is yet further appreciated that a function of VGAM692 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM692 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM692 correlate with, and may be deduced from, the identity of the host target genes which VGAM692 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9653] Nucleotide sequences of the VGAM692 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM692 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM692 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM692 are further described hereinbelow with reference to Table 1.

[9654] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM692 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9655] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 693 (VGAM693) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9656] VGAM693 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM693 was detected is described hereinabove with reference to Figs. 2-8.

[9657] VGAM693 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM693 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9658] VGAM693 gene, herein designated VGAM GENE, encodes a VGAM693 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM693 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM693 precursor RNA is designated SEQ ID:17546, and is provided hereinbelow with reference to the sequence listing part.

[9659] VGAM693 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM693 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9660] An enzyme complex designated DICER COMPLEX, dices the VGAM693 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM693 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM693 RNA is designated SEQ ID:17547, and is provided hereinbelow with reference to the sequence listing part.

[9661] VGAM693 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM693 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM693 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9662] VGAM693 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM693 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM693 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM693 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM693 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9663] The complementary binding of VGAM693 RNA, herein designated VGAM RNA, to host target binding sites on VGAM693 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM693 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM693 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9664] It is appreciated that VGAM693 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM693 host target genes. The mRNA of each one of this plurality of VGAM693 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM693 RNA, herein designated VGAM RNA, and which when bound by VGAM693 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM693 host target proteins.

[9665] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM693 gene, herein designated VGAM GENE, on one or more VGAM693 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9666] It is yet further appreciated that a function of VGAM693 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM693 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM693 correlate with, and may be deduced from, the identity of the host target genes which VGAM693 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9667] Nucleotide sequences of the VGAM693 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM693 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM693 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM693 are further described hereinbelow with reference to Table 1.

[9668] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM693 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9669] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 694 (VGAM694) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9670] VGAM694 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM694 was detected is described hereinabove with reference to Figs. 2-8.

[9671] VGAM694 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM694 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[9672] VGAM694 gene, herein designated VGAM GENE, encodes a VGAM694 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM694 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM694 precursor RNA is designated SEQ ID:17629, and is provided hereinbelow with reference to the sequence listing part.

[9673] VGAM694 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM694 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9674] An enzyme complex designated DICER COMPLEX, dices the VGAM694 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM694 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM694 RNA is designated SEQ ID:17630, and is provided hereinbelow with reference to the sequence listing part.

[9675] VGAM694 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM694 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM694 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9676] VGAM694 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM694 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM694 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM694 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM694 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9677] The complementary binding of VGAM694 RNA, herein designated VGAM RNA, to host target binding sites on VGAM694 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM694 host target RNA, herein designated VGAM HOST TARGET RNA,



into VGAM694 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9678] It is appreciated that VGAM694 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM694 host target genes. The mRNA of each one of this plurality of VGAM694 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM694 RNA, herein designated VGAM RNA, and which when bound by VGAM694 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM694 host target proteins.

[9679] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM694 gene, herein designated VGAM GENE, on one or more VGAM694 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9680] It is yet further appreciated that a function of VGAM694 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM694 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM694 correlate with, and may be deduced from, the identity of the host target genes which VGAM694 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9681] Nucleotide sequences of the VGAM694 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM694 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM694 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM694 are further de-

scribed hereinbelow with reference to Table 1.

[9682] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM694 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9683] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 695 (VGAM695) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9684] VGAM695 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM695 was detected is described hereinabove with reference to Figs. 2-8.

[9685] VGAM695 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM695 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9686] VGAM695 gene, herein designated VGAM GENE, encodes a VGAM695 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM695 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM695 precursor RNA is designated SEQ ID:17685, and is provided hereinbelow with reference to the sequence listing part.

[9687] VGAM695 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM695 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9688] An enzyme complex designated DICER COMPLEX, dices the VGAM695 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM695 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM695 RNA is designated SEQ ID:17686, and is provided hereinbelow with reference to the sequence listing part.

[9689] VGAM695 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM695 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM695 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9690] VGAM695 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM695 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM695 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM695 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM695 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9691] The complementary binding of VGAM695 RNA, herein designated VGAM RNA, to host target binding sites on VGAM695 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM695 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM695 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9692] It is appreciated that VGAM695 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM695 host target genes. The mRNA of each one of this plurality of VGAM695 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM695 RNA, herein designated VGAM RNA, and which when bound by VGAM695 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM695 host target proteins.

[9693] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM695 gene, herein designated VGAM GENE, on one or more VGAM695 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9694] It is yet further appreciated that a function of VGAM695 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM695 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM695 correlate with, and may be deduced from, the identity of the host target genes which VGAM695 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9695] Nucleotide sequences of the VGAM695 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM695 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM695 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM695 are further described hereinbelow with reference to Table 1.



[9696] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM695 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9697] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 696 (VGAM696) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9698] VGAM696 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM696 was detected is described hereinabove with reference to Figs. 2-8.

[9699] VGAM696 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM696 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9700] VGAM696 gene, herein designated VGAM GENE, encodes a

VGAM696 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM696 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM696 precursor RNA is designated SEQ ID:17718, and is provided hereinbelow with reference to the sequence listing part.

[9701] VGAM696 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM696 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9702] An enzyme complex designated DICER COMPLEX, dices the VGAM696 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM696 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM696 RNA is designated SEQ ID:17719, and is provided hereinbelow with reference to the sequence listing part.

[9703] VGAM696 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM696 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM696 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9704] VGAM696 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM696 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM696 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM696 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM696 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9705] The complementary binding of VGAM696 RNA, herein designated VGAM RNA, to host target binding sites on VGAM696 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM696 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM696 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[9706] It is appreciated that VGAM696 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM696 host target genes. The mRNA of each one of this plurality of VGAM696 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM696 RNA, herein designated VGAM RNA, and which when bound by VGAM696 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM696 host target proteins.

[9707] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM696 gene, herein designated VGAM GENE, on one or more VGAM696 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9708] It is yet further appreciated that a function of VGAM696 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM696 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM696 correlate with, and may be deduced from, the identity of the host target genes which VGAM696 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9709] Nucleotide sequences of the VGAM696 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM696 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM696 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM696 are further described hereinbelow with reference to Table 1.

[9710] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM696 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9711] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 697 (VGAM697) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9712] VGAM697 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM697 was detected is described hereinabove with reference to Figs. 2-8.

[9713] VGAM697 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM697 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9714] VGAM697 gene, herein designated VGAM GENE, encodes a VGAM697 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM697 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM697 precursor RNA is designated SEQ ID:17725, and is provided hereinbelow with reference to the sequence listing part.

[9715] VGAM697 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM697 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9716] An enzyme complex designated DICER COMPLEX, dices the VGAM697 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM697 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM697 RNA is designated SEQ ID:17726, and is provided hereinbelow with reference to the sequence listing part.

[9717] VGAM697 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM697 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM697 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9718] VGAM697 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM697 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM697 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM697 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM697 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9719] The complementary binding of VGAM697 RNA, herein designated VGAM RNA, to host target binding sites on VGAM697 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM697 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM697 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9720] It is appreciated that VGAM697 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM697 host target genes. The mRNA of each one of this plurality of VGAM697 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM697 RNA, herein designated VGAM RNA, and which when bound by VGAM697 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM697 host target proteins.

[9721] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM697 gene, herein designated VGAM GENE, on one or more VGAM697 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9722] It is yet further appreciated that a function of VGAM697 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM697 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM697 correlate with, and may be deduced from, the identity of the host target genes which VGAM697 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9723] Nucleotide sequences of the VGAM697 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM697 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM697 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM697 are further described hereinbelow with reference to Table 1.

[9724] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM697 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9725] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 698 (VGAM698) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9726] VGAM698 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM698 was detected is described hereinabove with reference to Figs. 2–8.

[9727] VGAM698 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM698 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9728] VGAM698 gene, herein designated VGAM GENE, encodes a VGAM698 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM698 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM698 precursor RNA is designated SEQ ID:17740, and is provided hereinbelow with reference to the sequence listing part.

[9729] VGAM698 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM698 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9730] An enzyme complex designated DICER COMPLEX, dices the VGAM698 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM698 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM698 RNA is designated SEQ ID:17741, and is provided hereinbelow with reference to the sequence listing part.

[9731] VGAM698 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM698 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM698 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9732] VGAM698 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM698 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM698 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM698 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM698 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9733] The complementary binding of VGAM698 RNA, herein designated VGAM RNA, to host target binding sites on VGAM698 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM698 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM698 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9734] It is appreciated that VGAM698 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM698 host target genes. The mRNA of each one of this plurality of VGAM698 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM698 RNA, herein designated VGAM RNA, and which when bound by VGAM698 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM698 host target proteins.

[9735] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM698 gene, herein designated VGAM GENE, on one or more VGAM698 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9736] It is yet further appreciated that a function of VGAM698 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM698 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM698 correlate with, and may be deduced from, the identity of the host target genes which VGAM698 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9737] Nucleotide sequences of the VGAM698 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM698 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM698 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM698 are further described hereinbelow with reference to Table 1.

[9738] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM698 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9739] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 699 (VGAM699) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9740] VGAM699 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM699 was detected is described hereinabove with reference to Figs. 2–8.

[9741] VGAM699 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM699 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9742] VGAM699 gene, herein designated VGAM GENE, encodes a VGAM699 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM699 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM699 precursor RNA is designated SEQ ID:17748, and is provided hereinbelow with reference to the sequence listing part.

[9743] VGAM699 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM699 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9744] An enzyme complex designated DICER COMPLEX, dices the VGAM699 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM699 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM699 RNA is designated SEQ ID:17749, and is provided hereinbelow with reference to the sequence listing part.

[9745] VGAM699 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM699 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM699 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9746] VGAM699 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM699 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM699 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM699 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM699 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9747] The complementary binding of VGAM699 RNA, herein designated VGAM RNA, to host target binding sites on VGAM699 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM699 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM699 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9748] It is appreciated that VGAM699 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM699 host target genes. The mRNA of each one of this plurality of VGAM699 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM699 RNA, herein designated VGAM RNA, and which when bound by VGAM699 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM699 host target proteins.

[9749] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM699 gene, herein designated VGAM GENE, on one or more VGAM699 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[9750] It is yet further appreciated that a function of VGAM699 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM699 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM699 correlate with, and may be deduced from, the identity of the host target genes which VGAM699 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9751] Nucleotide sequences of the VGAM699 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM699 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM699 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM699 are further described hereinbelow with reference to Table 1.

[9752] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM699 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9753] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 700 (VGAM700) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9754] VGAM700 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM700 was detected is described hereinabove with reference to Figs. 2–8.

[9755] VGAM700 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 32. VGAM700 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9756] VGAM700 gene, herein designated VGAM GENE, encodes a VGAM700 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM700 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM700 precursor RNA is designated SEQ ID:17756, and is provided hereinbelow with reference to the sequence listing part.

[9757] VGAM700 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM700 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9758] An enzyme complex designated DICER COMPLEX, dices the VGAM700 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM700 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM700 RNA is designated SEQ ID:17757, and is provided hereinbelow with reference to the sequence listing part.

[9759] VGAM700 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM700 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM700 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9760] VGAM700 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM700 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM700 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM700 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM700 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9761] The complementary binding of VGAM700 RNA, herein designated VGAM RNA, to host target binding sites on VGAM700 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM700 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM700 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9762] It is appreciated that VGAM700 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM700 host target genes. The mRNA of

each one of this plurality of VGAM700 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM700 RNA, herein designated VGAM RNA, and which when bound by VGAM700 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM700 host target proteins.

[9763] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM700 gene, herein designated VGAM GENE, on one or more VGAM700 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[9764] It is yet further appreciated that a function of VGAM700 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM700 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 32. Specific functions, and accordingly utilities, of VGAM700 correlate with, and may be deduced from, the identity of the host target genes which VGAM700 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9765] Nucleotide sequences of the VGAM700 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM700 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM700 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM700 are further described hereinbelow with reference to Table 1.

[9766] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM700 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[9767] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 701 (VGAM701) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9768] VGAM701 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM701 was detected is described hereinabove with reference to Figs. 2–8.

[9769] VGAM701 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM701 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9770] VGAM701 gene, herein designated VGAM GENE, encodes a VGAM701 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM701 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM701 precursor RNA is designated SEQ ID:17797, and is provided hereinbelow with reference to the sequence listing part.

[9771] VGAM701 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM701 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9772] An enzyme complex designated DICER COMPLEX, dices the VGAM701 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM701 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM701 RNA is designated SEQ ID:17798, and



is provided hereinbelow with reference to the sequence listing part.

[9773] VGAM701 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM701 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM701 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9774] VGAM701 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM701 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM701 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM701 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM701 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9775] The complementary binding of VGAM701 RNA, herein designated VGAM RNA, to host target binding sites on VGAM701 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM701 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM701 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9776] It is appreciated that VGAM701 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM701 host target genes. The mRNA of each one of this plurality of VGAM701 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM701 RNA, herein designated VGAM RNA, and which when bound by VGAM701 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM701 host target proteins.

[9777] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM701 gene, herein designated VGAM GENE, on one or more VGAM701 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9778] It is yet further appreciated that a function of VGAM701 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM701 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM701 correlate with, and may be deduced from, the identity of the host target genes which VGAM701 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9779] Nucleotide sequences of the VGAM701 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM701 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM701 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM701 are further described hereinbelow with reference to Table 1.

[9780] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM701 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9781] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 702 (VGAM702) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9782] VGAM702 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM702 was detected is described hereinabove with reference to Figs. 2–8.

[9783] VGAM702 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 32. VGAM702 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9784] VGAM702 gene, herein designated VGAM GENE, encodes a VGAM702 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM702 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM702 precursor RNA is

designated SEQ ID:17844, and is provided hereinbelow with reference to the sequence listing part.

[9785] VGAM702 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM702 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9786] An enzyme complex designated DICER COMPLEX, dices the VGAM702 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM702 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM702 RNA is designated SEQ ID:17845, and is provided hereinbelow with reference to the sequence

listing part.

[9787] VGAM702 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM702 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM702 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9788] VGAM702 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM702 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM702 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM702 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM702 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9789] The complementary binding of VGAM702 RNA, herein designated VGAM RNA, to host target binding sites on VGAM702 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM702 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM702 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9790] It is appreciated that VGAM702 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM702 host target genes. The mRNA of each one of this plurality of VGAM702 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM702 RNA, herein designated VGAM RNA, and which when bound by VGAM702 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM702 host target proteins.

[9791] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM702 gene, herein designated VGAM GENE, on one or more VGAM702 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9792] It is yet further appreciated that a function of VGAM702 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM702 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 32. Specific functions, and accordingly utilities, of VGAM702 correlate with, and may be deduced from, the identity of the host target genes which VGAM702 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9793] Nucleotide sequences of the VGAM702 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM702 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM702 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM702 are further described hereinbelow with reference to Table 1.

[9794] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM702 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9795] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 703 (VGAM703) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9796] VGAM703 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM703 was detected is described hereinabove with reference to Figs. 2–8.

[9797] VGAM703 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM703 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9798] VGAM703 gene, herein designated VGAM GENE, encodes a VGAM703 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM703 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM703 precursor RNA is designated SEQ ID:17849, and is provided hereinbelow

with reference to the sequence listing part.

[9799] VGAM703 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM703 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9800] An enzyme complex designated DICER COMPLEX, dices the VGAM703 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM703 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM703 RNA is designated SEQ ID:17850, and is provided hereinbelow with reference to the sequence listing part.

[9801] VGAM703 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM703 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM703 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9802] VGAM703 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM703 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM703 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM703 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM703 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9803] The complementary binding of VGAM703 RNA, herein designated VGAM RNA, to host target binding sites on VGAM703 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM703 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM703 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9804] It is appreciated that VGAM703 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM703 host target genes. The mRNA of each one of this plurality of VGAM703 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM703 RNA, herein designated VGAM RNA, and which when bound by VGAM703 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM703 host target proteins.

[9805] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM703 gene, herein designated VGAM GENE, on one or more VGAM703 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9806] It is yet further appreciated that a function of VGAM703 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM703 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM703 correlate with, and may be deduced from, the identity of the host target genes which VGAM703 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9807] Nucleotide sequences of the VGAM703 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM703 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM703 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM703 are further described hereinbelow with reference to Table 1.

[9808] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM703 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9809] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 704 (VGAM704) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9810] VGAM704 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM704 was detected is described hereinabove with reference to Figs. 2–8.

[9811] VGAM704 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM704 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9812] VGAM704 gene, herein designated VGAM GENE, encodes a VGAM704 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM704 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM704 precursor RNA is designated SEQ ID:17868, and is provided hereinbelow with reference to the sequence listing part.

[9813] VGAM704 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM704 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9814] An enzyme complex designated DICER COMPLEX, dices the VGAM704 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM704 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM704 RNA is designated SEQ ID:17869, and is provided hereinbelow with reference to the sequence listing part.

[9815] VGAM704 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM704 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM704 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9816] VGAM704 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM704 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM704 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM704 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM704 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9817] The complementary binding of VGAM704 RNA, herein designated VGAM RNA, to host target binding sites on VGAM704 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM704 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM704 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9818] It is appreciated that VGAM704 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM704 host target genes. The mRNA of each one of this plurality of VGAM704 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM704 RNA, herein designated VGAM

RNA, and which when bound by VGAM704 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM704 host target proteins.

[9819] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM704 gene, herein designated VGAM GENE, on one or more VGAM704 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9820] It is yet further appreciated that a function of VGAM704 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM704 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM704 correlate with, and may be deduced from, the identity of the host target genes which VGAM704 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9821] Nucleotide sequences of the VGAM704 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM704 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM704 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM704 are further described hereinbelow with reference to Table 1.

[9822] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM704 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9823] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 705 (VGAM705) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9824] VGAM705 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM705 was detected is described hereinabove with reference to Figs. 2–8.

[9825] VGAM705 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM705 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9826] VGAM705 gene, herein designated VGAM GENE, encodes a VGAM705 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM705 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM705 precursor RNA is designated SEQ ID:17872, and is provided hereinbelow with reference to the sequence listing part.

[9827] VGAM705 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM705 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9828] An enzyme complex designated DICER COMPLEX, dices the VGAM705 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM705 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM705 RNA is designated SEQ ID:17873, and is provided hereinbelow with reference to the sequence listing part.

[9829] VGAM705 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM705 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM705 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9830] VGAM705 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM705 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM705 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM705 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM705 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9831] The complementary binding of VGAM705 RNA, herein designated VGAM RNA, to host target binding sites on VGAM705 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM705 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM705 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9832] It is appreciated that VGAM705 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM705 host target genes. The mRNA of each one of this plurality of VGAM705 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM705 RNA, herein designated VGAM RNA, and which when bound by VGAM705 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM705 host target proteins.

[9833] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM705 gene, herein designated VGAM GENE, on one or more VGAM705 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9834] It is yet further appreciated that a function of VGAM705 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM705 include diagnosis, prevention and

treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM705 correlate with, and may be deduced from, the identity of the host target genes which VGAM705 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9835] Nucleotide sequences of the VGAM705 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM705 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM705 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM705 are further described hereinbelow with reference to Table 1.

[9836] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM705 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9837] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 706 (VGAM706) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9838] VGAM706 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM706 was detected is described hereinabove with reference to Figs. 2–8.

[9839] VGAM706 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM706 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9840] VGAM706 gene, herein designated VGAM GENE, encodes a VGAM706 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM706 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM706 precursor RNA is designated SEQ ID:17903, and is provided hereinbelow with reference to the sequence listing part.

[9841] VGAM706 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM706 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9842] An enzyme complex designated DICER COMPLEX, dices the VGAM706 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM706 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM706 RNA is designated SEQ ID:17904, and is provided hereinbelow with reference to the sequence listing part.

[9843] VGAM706 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM706 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM706 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9844] VGAM706 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM706 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM706 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM706 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM706 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9845] The complementary binding of VGAM706 RNA, herein designated VGAM RNA, to host target binding sites on VGAM706 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM706 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM706 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9846] It is appreciated that VGAM706 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM706 host target genes. The mRNA of each one of this plurality of VGAM706 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM706 RNA, herein designated VGAM RNA, and which when bound by VGAM706 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM706 host target proteins.

[9847] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM706 gene, herein designated VGAM GENE, on one or more VGAM706 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9848] It is yet further appreciated that a function of VGAM706 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM706 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Spe-

cific functions, and accordingly utilities, of VGAM706 correlate with, and may be deduced from, the identity of the host target genes which VGAM706 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9849] Nucleotide sequences of the VGAM706 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM706 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM706 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM706 are further described hereinbelow with reference to Table 1.

[9850] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM706 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9851] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 707 (VGAM707) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[9852] VGAM707 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM707 was detected is described hereinabove with reference to Figs. 2–8.

[9853] VGAM707 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM707 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9854] VGAM707 gene, herein designated VGAM GENE, encodes a VGAM707 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM707 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM707 precursor RNA is designated SEQ ID:17922, and is provided hereinbelow with reference to the sequence listing part.

[9855] VGAM707 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM707 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9856] An enzyme complex designated DICER COMPLEX, dices the VGAM707 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM707 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM707 RNA is designated SEQ ID:17923, and is provided hereinbelow with reference to the sequence listing part.

[9857] VGAM707 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM707 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM707 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9858] VGAM707 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM707 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM707 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM707 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM707 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9859] The complementary binding of VGAM707 RNA, herein designated VGAM RNA, to host target binding sites on VGAM707 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM707 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM707 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9860] It is appreciated that VGAM707 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM707 host target genes. The mRNA of each one of this plurality of VGAM707 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM707 RNA, herein designated VGAM RNA, and which when bound by VGAM707 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM707 host target proteins.

[9861] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM707 gene, herein designated VGAM GENE, on one or more VGAM707 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9862] It is yet further appreciated that a function of VGAM707 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM707 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM707

correlate with, and may be deduced from, the identity of the host target genes which VGAM707 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9863] Nucleotide sequences of the VGAM707 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM707 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM707 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM707 are further described hereinbelow with reference to Table 1.

[9864] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM707 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9865] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 708 (VGAM708) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[9866] VGAM708 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM708 was detected is described hereinabove with reference to Figs. 2–8.

[9867] VGAM708 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM708 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9868] VGAM708 gene, herein designated VGAM GENE, encodes a VGAM708 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM708 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM708 precursor RNA is designated SEQ ID:17953, and is provided hereinbelow with reference to the sequence listing part.

[9869] VGAM708 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM708 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9870] An enzyme complex designated DICER COMPLEX, dices the VGAM708 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM708 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM708 RNA is designated SEQ ID:17954, and is provided hereinbelow with reference to the sequence listing part.

[9871] VGAM708 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM708 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM708 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9872] VGAM708 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM708 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM708 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM708 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM708 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9873] The complementary binding of VGAM708 RNA, herein designated VGAM RNA, to host target binding sites on VGAM708 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM708 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM708 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9874] It is appreciated that VGAM708 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM708 host target genes. The mRNA of each one of this plurality of VGAM708 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM708 RNA, herein designated VGAM RNA, and which when bound by VGAM708 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM708 host target proteins.

[9875] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM708 gene, herein designated VGAM GENE, on one or more VGAM708 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9876] It is yet further appreciated that a function of VGAM708 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM708 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM708 correlate with, and may be deduced from, the identity of

the host target genes which VGAM708 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9877] Nucleotide sequences of the VGAM708 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM708 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM708 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM708 are further described hereinbelow with reference to Table 1.

[9878] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM708 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9879] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 709 (VGAM709) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9880] VGAM709 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM709 was detected is described hereinabove with reference to Figs. 2–8.

[9881] VGAM709 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM709 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9882] VGAM709 gene, herein designated VGAM GENE, encodes a VGAM709 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM709 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM709 precursor RNA is designated SEQ ID:17971, and is provided hereinbelow with reference to the sequence listing part.

[9883] VGAM709 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM709 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9884] An enzyme complex designated DICER COMPLEX, dices the VGAM709 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM709 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM709 RNA is designated SEQ ID:17972, and is provided hereinbelow with reference to the sequence listing part.

[9885] VGAM709 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM709 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM709 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5



untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9886] VGAM709 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM709 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM709 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM709 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM709 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9887] The complementary binding of VGAM709 RNA, herein designated VGAM RNA, to host target binding sites on VGAM709 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM709 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM709 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9888] It is appreciated that VGAM709 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM709 host target genes. The mRNA of each one of this plurality of VGAM709 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM709 RNA, herein designated VGAM RNA, and which when bound by VGAM709 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM709 host target proteins.

[9889] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM709 gene, herein designated VGAM GENE, on one or more VGAM709 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9890] It is yet further appreciated that a function of VGAM709 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM709 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM709 correlate with, and may be deduced from, the identity of the host target genes which VGAM709 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[9891] Nucleotide sequences of the VGAM709 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM709 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM709 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM709 are further described hereinbelow with reference to Table 1.

[9892] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM709 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9893] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 710 (VGAM710) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9894] VGAM710 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM710 was detected is described hereinabove with reference to Figs. 2–8.

[9895] VGAM710 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM710 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9896] VGAM710 gene, herein designated VGAM GENE, encodes a VGAM710 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM710 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM710 precursor RNA is designated SEQ ID:18028, and is provided hereinbelow with reference to the sequence listing part.

[9897] VGAM710 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM710 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9898] An enzyme complex designated DICER COMPLEX, dices the VGAM710 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM710 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM710 RNA is designated SEQ ID:18029, and is provided hereinbelow with reference to the sequence listing part.

[9899] VGAM710 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM710 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM710 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9900] VGAM710 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM710 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM710 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM710 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM710 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[9901] The complementary binding of VGAM710 RNA, herein designated VGAM RNA, to host target binding sites on VGAM710 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM710 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM710 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9902] It is appreciated that VGAM710 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM710 host target genes. The mRNA of each one of this plurality of VGAM710 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM710 RNA, herein designated VGAM RNA, and which when bound by VGAM710 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM710 host target proteins.

[9903] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM710 gene, herein designated VGAM GENE, on one or more VGAM710 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9904] It is yet further appreciated that a function of VGAM710 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM710 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM710 correlate with, and may be deduced from, the identity of the host target genes which VGAM710 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[9905] Nucleotide sequences of the VGAM710 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM710 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM710 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM710 are further described hereinbelow with reference to Table 1.

[9906] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM710 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9907] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 711 (VGAM711) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9908] VGAM711 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM711 was detected is described hereinabove with reference to Figs. 2–8.

[9909] VGAM711 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM711 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9910] VGAM711 gene, herein designated VGAM GENE, encodes a VGAM711 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM711 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM711 precursor RNA is designated SEQ ID:18047, and is provided hereinbelow with reference to the sequence listing part.

[9911] VGAM711 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM711 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9912] An enzyme complex designated DICER COMPLEX, dices the VGAM711 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM711 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM711 RNA is designated SEQ ID:18048, and is provided hereinbelow with reference to the sequence listing part.

[9913] VGAM711 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM711 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM711 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[9914] VGAM711 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM711 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM711 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM711 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM711 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9915] The complementary binding of VGAM711 RNA, herein designated VGAM RNA, to host target binding sites on VGAM711 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM711 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM711 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9916] It is appreciated that VGAM711 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM711 host target genes. The mRNA of each one of this plurality of VGAM711 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM711 RNA, herein designated VGAM RNA, and which when bound by VGAM711 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM711 host target proteins.

[9917] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM711 gene, herein designated VGAM GENE, on one or

more VGAM711 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9918] It is yet further appreciated that a function of VGAM711 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM711 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM711 correlate with, and may be deduced from, the identity of the host target genes which VGAM711 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9919] Nucleotide sequences of the VGAM711 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM711 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM711 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM711 are further described hereinbelow with reference to Table 1.

[9920] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM711 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9921] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 712 (VGAM712) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9922] VGAM712 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM712 was detected is described



hereinabove with reference to Figs. 2–8.

[9923] VGAM712 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM712 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9924] VGAM712 gene, herein designated VGAM GENE, encodes a VGAM712 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM712 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM712 precursor RNA is designated SEQ ID:18533, and is provided hereinbelow with reference to the sequence listing part.

[9925] VGAM712 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM712 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9926] An enzyme complex designated DICER COMPLEX, dices the VGAM712 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM712 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM712 RNA is designated SEQ ID:18534, and is provided hereinbelow with reference to the sequence listing part.

[9927] VGAM712 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM712 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM712 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9928] VGAM712 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM712 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM712 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM712 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM712 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9929] The complementary binding of VGAM712 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM712 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM712 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM712 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9930] It is appreciated that VGAM712 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM712 host target genes. The mRNA of each one of this plurality of VGAM712 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM712 RNA, herein designated VGAM RNA, and which when bound by VGAM712 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM712 host target proteins.

[9931] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM712 gene, herein designated VGAM GENE, on one or more VGAM712 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9932] It is yet further appreciated that a function of VGAM712 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM712 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM712 correlate with, and may be deduced from, the identity of the host target genes which VGAM712 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9933] Nucleotide sequences of the VGAM712 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM712 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM712 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM712 are further described hereinbelow with reference to Table 1.

[9934] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM712 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9935] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 713 (VGAM713) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9936] VGAM713 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM713 was detected is described hereinabove with reference to Figs. 2-8.

[9937] VGAM713 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM713 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9938] VGAM713 gene, herein designated VGAM GENE, encodes a VGAM713 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM713 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM713 precursor RNA is designated SEQ ID:18557, and is provided hereinbelow with reference to the sequence listing part.

[9939] VGAM713 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM713 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[9940] An enzyme complex designated DICER COMPLEX, dices the VGAM713 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM713 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM713 RNA is designated SEQ ID:18558, and is provided hereinbelow with reference to the sequence listing part.

[9941] VGAM713 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM713 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM713 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9942] VGAM713 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM713 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM713 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM713 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM713 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9943] The complementary binding of VGAM713 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM713 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM713 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM713 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9944] It is appreciated that VGAM713 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM713 host target genes. The mRNA of each one of this plurality of VGAM713 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM713 RNA, herein designated VGAM RNA, and which when bound by VGAM713 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM713 host target proteins.

[9945] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM713 gene, herein designated VGAM GENE, on one or more VGAM713 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9946] It is yet further appreciated that a function of VGAM713 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM713 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM713 correlate with, and may be deduced from, the identity of the host target genes which VGAM713 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9947] Nucleotide sequences of the VGAM713 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM713 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM713 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM713 are further described hereinbelow with reference to Table 1.

[9948] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM713 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9949] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 714 (VGAM714) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9950] VGAM714 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM714 was detected is described hereinabove with reference to Figs. 2-8.

[9951] VGAM714 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Chimpanzee cytomegalovirus. VGAM714 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9952] VGAM714 gene, herein designated VGAM GENE, encodes a VGAM714 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM714 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM714 precursor RNA is designated SEQ ID:18576, and is provided hereinbelow with reference to the sequence listing part.

[9953] VGAM714 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM714 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9954] An enzyme complex designated DICER COMPLEX, dices the VGAM714 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM714 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM714 RNA is designated SEQ ID:18577, and is provided hereinbelow with reference to the sequence listing part.

[9955] VGAM714 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM714 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM714 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9956] VGAM714 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM714 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM714 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM714 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM714 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9957] The complementary binding of VGAM714 RNA, herein designated VGAM RNA, to host target binding sites on VGAM714 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM714 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM714 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9958] It is appreciated that VGAM714 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM714 host target genes. The mRNA of each one of this plurality of VGAM714 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM714 RNA, herein designated VGAM RNA, and which when bound by VGAM714 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM714 host target proteins.

[9959] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM714 gene, herein designated VGAM GENE, on one or more VGAM714 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9960] It is yet further appreciated that a function of VGAM714 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM714 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM714 correlate with, and may be deduced from, the identity of the host target genes which VGAM714 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9961] Nucleotide sequences of the VGAM714 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM714 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM714 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM714 are further described hereinbelow with reference to Table 1.

[9962] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM714 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9963] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 715 (VGAM715) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9964] VGAM715 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM715 was detected is described hereinabove with reference to Figs. 2-8.

[9965] VGAM715 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cy-

tomegalovirus. VGAM715 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9966] VGAM715 gene, herein designated VGAM GENE, encodes a VGAM715 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM715 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM715 precursor RNA is designated SEQ ID:18594, and is provided hereinbelow with reference to the sequence listing part.

[9967] VGAM715 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM715 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9968] An enzyme complex designated DICER COMPLEX, dices

the VGAM715 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM715 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM715 RNA is designated SEQ ID:18595, and is provided hereinbelow with reference to the sequence listing part.

[9969] VGAM715 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM715 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM715 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9970] VGAM715 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM715 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM715 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM715 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM715 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9971] The complementary binding of VGAM715 RNA, herein designated VGAM RNA, to host target binding sites on VGAM715 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM715 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM715 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9972] It is appreciated that VGAM715 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM715 host target genes. The mRNA of each one of this plurality of VGAM715 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM715 RNA, herein designated VGAM RNA, and which when bound by VGAM715 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM715 host target proteins.

[9973] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM715 gene, herein designated VGAM GENE, on one or more VGAM715 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9974] It is yet further appreciated that a function of VGAM715 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM715 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM715 correlate with, and may be deduced from, the identity of the host target genes which VGAM715 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9975] Nucleotide sequences of the VGAM715 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM715 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM715 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM715 are further described hereinbelow with reference to Table 1.

[9976] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM715 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9977] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 716 (VGAM716) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9978] VGAM716 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM716 was detected is described hereinabove with reference to Figs. 2-8.

[9979] VGAM716 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Borna disease virus. VGAM716 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[9980] VGAM716 gene, herein designated VGAM GENE, encodes a VGAM716 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM716 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM716 precursor RNA is designated SEQ ID:18729, and is provided hereinbelow with reference to the sequence listing part.

[9981] VGAM716 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM716 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9982] An enzyme complex designated DICER COMPLEX, dices the VGAM716 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM716 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM716 RNA is designated SEQ ID:18730, and is provided hereinbelow with reference to the sequence listing part.

[9983] VGAM716 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM716 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM716 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9984] VGAM716 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM716 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM716 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM716 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM716 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9985] The complementary binding of VGAM716 RNA, herein designated VGAM RNA, to host target binding sites on VGAM716 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM716 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM716 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9986] It is appreciated that VGAM716 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM716 host target genes. The mRNA of each one of this plurality of VGAM716 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM716 RNA, herein designated VGAM RNA, and which when bound by VGAM716 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM716 host target proteins.

[9987] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM716 gene, herein designated VGAM GENE, on one or more VGAM716 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[9988] It is yet further appreciated that a function of VGAM716 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM716 include diagnosis, prevention and treatment of viral infection by Borna disease virus. Specific functions, and accordingly utilities, of VGAM716 correlate with, and may be deduced from, the identity of the host target genes which VGAM716 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9989] Nucleotide sequences of the VGAM716 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM716 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM716 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM716 are further described hereinbelow with reference to Table 1.

[9990] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM716 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9991] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 717 (VGAM717) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9992] VGAM717 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM717 was detected is described hereinabove with reference to Figs. 2-8.

[9993] VGAM717 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine immunodeficiency virus. VGAM717 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[9994] VGAM717 gene, herein designated VGAM GENE, encodes a VGAM717 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM717 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM717 precursor RNA is designated SEQ ID:18841, and is provided hereinbelow with reference to the sequence listing part.

[9995] VGAM717 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM717 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9996] An enzyme complex designated DICER COMPLEX, dices the VGAM717 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM717 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM717 RNA is designated SEQ ID:18842, and is provided hereinbelow with reference to the sequence listing part.

[9997] VGAM717 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM717 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM717 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[9998] VGAM717 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM717 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM717 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM717 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM717 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[9999] The complementary binding of VGAM717 RNA, herein designated VGAM RNA, to host target binding sites on VGAM717 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM717 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM717 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10000] It is appreciated that VGAM717 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM717 host target genes. The mRNA of each one of this plurality of VGAM717 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM717 RNA, herein designated VGAM RNA, and which when bound by VGAM717 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM717 host target proteins.

[10001] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM717 gene, herein designated VGAM GENE, on one or more VGAM717 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10002] It is yet further appreciated that a function of VGAM717 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM717 include diagnosis, prevention and treatment of viral infection by Bovine immunodeficiency virus. Specific functions, and accordingly utilities, of VGAM717 correlate with, and may be deduced from, the identity of the host target genes which VGAM717 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10003] Nucleotide sequences of the VGAM717 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM717 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM717 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM717 are further de-

scribed hereinbelow with reference to Table 1.

[10004] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM717 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10005] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 718 (VGAM718) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10006] VGAM718 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM718 was detected is described hereinabove with reference to Figs. 2-8.

[10007] VGAM718 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine immunodeficiency virus. VGAM718 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10008] VGAM718 gene, herein designated VGAM GENE, encodes a VGAM718 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM718 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM718 precursor RNA is designated SEQ ID:18863, and is provided hereinbelow with reference to the sequence listing part.

[10009] VGAM718 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM718 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10010] An enzyme complex designated DICER COMPLEX, dices the VGAM718 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM718 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM718 RNA is designated SEQ ID:18864, and is provided hereinbelow with reference to the sequence listing part.

[10011] VGAM718 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM718 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM718 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10012] VGAM718 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM718 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM718 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM718 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM718 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10013] The complementary binding of VGAM718 RNA, herein designated VGAM RNA, to host target binding sites on VGAM718 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM718 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM718 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10014] It is appreciated that VGAM718 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM718 host target genes. The mRNA of each one of this plurality of VGAM718 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM718 RNA, herein designated VGAM RNA, and which when bound by VGAM718 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM718 host target proteins.

[10015] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM718 gene, herein designated VGAM GENE, on one or more VGAM718 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10016] It is yet further appreciated that a function of VGAM718 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM718 include diagnosis, prevention and treatment of viral infection by Bovine immunodeficiency virus. Specific functions, and accordingly utilities, of VGAM718 correlate with, and may be deduced from, the identity of the host target genes which VGAM718 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10017] Nucleotide sequences of the VGAM718 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM718 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM718 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM718 are further described hereinbelow with reference to Table 1.

[10018] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM718 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10019] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 719 (VGAM719) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10020] VGAM719 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM719 was detected is described hereinabove with reference to Figs. 2-8.

[10021] VGAM719 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM719 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10022] VGAM719 gene, herein designated VGAM GENE, encodes a

VGAM719 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM719 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM719 precursor RNA is designated SEQ ID:18876, and is provided hereinbelow with reference to the sequence listing part.

[10023] VGAM719 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM719 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10024] An enzyme complex designated DICER COMPLEX, dices the VGAM719 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM719 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM719 RNA is designated SEQ ID:18877, and is provided hereinbelow with reference to the sequence listing part.

[10025] VGAM719 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM719 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM719 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10026] VGAM719 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM719 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM719 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM719 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM719 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10027] The complementary binding of VGAM719 RNA, herein designated VGAM RNA, to host target binding sites on VGAM719 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM719 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM719 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[10028] It is appreciated that VGAM719 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM719 host target genes. The mRNA of each one of this plurality of VGAM719 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM719 RNA, herein designated VGAM RNA, and which when bound by VGAM719 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM719 host target proteins.

[10029] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM719 gene, herein designated VGAM GENE, on one or more VGAM719 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10030] It is yet further appreciated that a function of VGAM719 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM719 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM719 correlate with, and may be deduced from, the identity of the host target genes which VGAM719 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10031] Nucleotide sequences of the VGAM719 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM719 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM719 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM719 are further described hereinbelow with reference to Table 1.

[10032] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM719 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10033] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 720 (VGAM720) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10034] VGAM720 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM720 was detected is described hereinabove with reference to Figs. 2-8.

[10035] VGAM720 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM720 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10036] VGAM720 gene, herein designated VGAM GENE, encodes a VGAM720 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM720 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM720 precursor RNA is designated SEQ ID:19130, and is provided hereinbelow with reference to the sequence listing part.

[10037] VGAM720 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM720 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10038] An enzyme complex designated DICER COMPLEX, dices the VGAM720 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM720 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM720 RNA is designated SEQ ID:19131, and is provided hereinbelow with reference to the sequence listing part.

[10039] VGAM720 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM720 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM720 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10040] VGAM720 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM720 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM720 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM720 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM720 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10041] The complementary binding of VGAM720 RNA, herein designated VGAM RNA, to host target binding sites on VGAM720 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM720 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM720 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10042] It is appreciated that VGAM720 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM720 host target genes. The mRNA of each one of this plurality of VGAM720 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM720 RNA, herein designated VGAM RNA, and which when bound by VGAM720 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM720 host target proteins.

[10043] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM720 gene, herein designated VGAM GENE, on one or more VGAM720 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10044] It is yet further appreciated that a function of VGAM720 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM720 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM720 correlate with, and may be deduced from, the identity of the host target genes which VGAM720 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10045] Nucleotide sequences of the VGAM720 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM720 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM720 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM720 are further described hereinbelow with reference to Table 1.

[10046] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM720 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10047] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 721 (VGAM721) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10048] VGAM721 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM721 was detected is described hereinabove with reference to Figs. 2–8.

[10049] VGAM721 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM721 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10050] VGAM721 gene, herein designated VGAM GENE, encodes a VGAM721 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM721 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM721 precursor RNA is designated SEQ ID:19217, and is provided hereinbelow with reference to the sequence listing part.

[10051] VGAM721 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM721 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10052] An enzyme complex designated DICER COMPLEX, dices the VGAM721 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM721 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM721 RNA is designated SEQ ID:19218, and is provided hereinbelow with reference to the sequence listing part.

[10053] VGAM721 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM721 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM721 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10054] VGAM721 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM721 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM721 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM721 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM721 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10055] The complementary binding of VGAM721 RNA, herein designated VGAM RNA, to host target binding sites on VGAM721 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM721 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM721 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10056] It is appreciated that VGAM721 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM721 host target genes. The mRNA of each one of this plurality of VGAM721 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM721 RNA, herein designated VGAM RNA, and which when bound by VGAM721 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM721 host target proteins.

[10057] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM721 gene, herein designated VGAM GENE, on one or more VGAM721 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10058] It is yet further appreciated that a function of VGAM721 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM721 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM721 correlate with, and may be deduced from, the identity of the host target genes which VGAM721 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10059] Nucleotide sequences of the VGAM721 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM721 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM721 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM721 are further described hereinbelow with reference to Table 1.

[10060] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM721 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10061] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 722 (VGAM722) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10062] VGAM722 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM722 was detected is described hereinabove with reference to Figs. 2–8.

[10063] VGAM722 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM722 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10064] VGAM722 gene, herein designated VGAM GENE, encodes a VGAM722 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM722 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM722 precursor RNA is designated SEQ ID:19339, and is provided hereinbelow with reference to the sequence listing part.

[10065] VGAM722 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM722 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10066] An enzyme complex designated DICER COMPLEX, dices the VGAM722 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM722 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM722 RNA is designated SEQ ID:19340, and is provided hereinbelow with reference to the sequence listing part.

[10067] VGAM722 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM722 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM722 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10068] VGAM722 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM722 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM722 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM722 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM722 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10069] The complementary binding of VGAM722 RNA, herein designated VGAM RNA, to host target binding sites on VGAM722 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM722 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM722 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10070] It is appreciated that VGAM722 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM722 host target genes. The mRNA of each one of this plurality of VGAM722 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM722 RNA, herein designated VGAM RNA, and which when bound by VGAM722 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM722 host target proteins.

[10071] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM722 gene, herein designated VGAM GENE, on one or more VGAM722 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[10072] It is yet further appreciated that a function of VGAM722 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM722 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM722 correlate with, and may be deduced from, the identity of the host target genes which VGAM722 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10073] Nucleotide sequences of the VGAM722 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM722 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM722 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM722 are further described hereinbelow with reference to Table 1.

[10074] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM722 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10075] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 723 (VGAM723) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10076] VGAM723 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM723 was detected is described hereinabove with reference to Figs. 2–8.

[10077] VGAM723 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM723 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10078] VGAM723 gene, herein designated VGAM GENE, encodes a VGAM723 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM723 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM723 precursor RNA is designated SEQ ID:19363, and is provided hereinbelow with reference to the sequence listing part.

[10079] VGAM723 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM723 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10080] An enzyme complex designated DICER COMPLEX, dices the VGAM723 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM723 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM723 RNA is designated SEQ ID:19364, and is provided hereinbelow with reference to the sequence listing part.

[10081] VGAM723 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM723 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM723 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10082] VGAM723 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM723 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM723 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM723 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM723 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10083] The complementary binding of VGAM723 RNA, herein designated VGAM RNA, to host target binding sites on VGAM723 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM723 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM723 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10084] It is appreciated that VGAM723 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM723 host target genes. The mRNA of

each one of this plurality of VGAM723 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM723 RNA, herein designated VGAM RNA, and which when bound by VGAM723 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM723 host target proteins.

[10085] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM723 gene, herein designated VGAM GENE, on one or more VGAM723 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[10086] It is yet further appreciated that a function of VGAM723 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM723 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM723 correlate with, and may be deduced from, the identity of the host target genes which VGAM723 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10087] Nucleotide sequences of the VGAM723 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM723 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM723 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM723 are further described hereinbelow with reference to Table 1.

[10088] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM723 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[10089] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 724 (VGAM724) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10090] VGAM724 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM724 was detected is described hereinabove with reference to Figs. 2–8.

[10091] VGAM724 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM724 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10092] VGAM724 gene, herein designated VGAM GENE, encodes a VGAM724 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM724 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar



to the nucleotide sequence of VGAM724 precursor RNA is designated SEQ ID:19511, and is provided hereinbelow with reference to the sequence listing part.

[10093] VGAM724 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM724 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10094] An enzyme complex designated DICER COMPLEX, dices the VGAM724 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM724 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM724 RNA is designated SEQ ID:19512, and

is provided hereinbelow with reference to the sequence listing part.

[10095] VGAM724 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM724 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM724 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10096] VGAM724 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM724 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM724 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM724 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM724 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10097] The complementary binding of VGAM724 RNA, herein designated VGAM RNA, to host target binding sites on VGAM724 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM724 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM724 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10098] It is appreciated that VGAM724 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM724 host target genes. The mRNA of each one of this plurality of VGAM724 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM724 RNA, herein designated VGAM RNA, and which when bound by VGAM724 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM724 host target proteins.

[10099] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM724 gene, herein designated VGAM GENE, on one or more VGAM724 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10100] It is yet further appreciated that a function of VGAM724 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM724 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM724 correlate with, and may be deduced from, the identity of the host target genes which VGAM724 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10101] Nucleotide sequences of the VGAM724 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM724 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM724 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM724 are further described hereinbelow with reference to Table 1.

[10102] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM724 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10103] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 725 (VGAM725) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10104] VGAM725 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM725 was detected is described hereinabove with reference to Figs. 2–8.

[10105] VGAM725 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM725 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10106] VGAM725 gene, herein designated VGAM GENE, encodes a VGAM725 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM725 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM725 precursor RNA is

designated SEQ ID:19528, and is provided hereinbelow with reference to the sequence listing part.

[10107] VGAM725 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM725 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10108] An enzyme complex designated DICER COMPLEX, dices the VGAM725 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM725 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM725 RNA is designated SEQ ID:19529, and is provided hereinbelow with reference to the sequence

listing part.

[10109] VGAM725 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM725 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM725 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10110] VGAM725 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM725 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM725 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM725 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM725 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10111] The complementary binding of VGAM725 RNA, herein designated VGAM RNA, to host target binding sites on VGAM725 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM725 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM725 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10112] It is appreciated that VGAM725 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM725 host target genes. The mRNA of each one of this plurality of VGAM725 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM725 RNA, herein designated VGAM RNA, and which when bound by VGAM725 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM725 host target proteins.

[10113] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM725 gene, herein designated VGAM GENE, on one or more VGAM725 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10114] It is yet further appreciated that a function of VGAM725 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM725 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM725 correlate with, and may be deduced from, the identity of the host target genes which VGAM725 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10115] Nucleotide sequences of the VGAM725 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM725 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM725 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM725 are further described hereinbelow with reference to Table 1.

[10116] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM725 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10117] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 726 (VGAM726) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10118] VGAM726 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM726 was detected is described hereinabove with reference to Figs. 2–8.

[10119] VGAM726 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM726 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10120] VGAM726 gene, herein designated VGAM GENE, encodes a VGAM726 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM726 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM726 precursor RNA is designated SEQ ID:19707, and is provided hereinbelow

with reference to the sequence listing part.

[10121] VGAM726 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM726 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10122] An enzyme complex designated DICER COMPLEX, dices the VGAM726 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM726 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM726 RNA is designated SEQ ID:19708, and is provided hereinbelow with reference to the sequence listing part.

[10123] VGAM726 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM726 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM726 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10124] VGAM726 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM726 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM726 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM726 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM726 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10125] The complementary binding of VGAM726 RNA, herein designated VGAM RNA, to host target binding sites on VGAM726 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM726 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM726 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10126] It is appreciated that VGAM726 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM726 host target genes. The mRNA of each one of this plurality of VGAM726 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM726 RNA, herein designated VGAM RNA, and which when bound by VGAM726 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM726 host target proteins.

[10127] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM726 gene, herein designated VGAM GENE, on one or more VGAM726 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10128] It is yet further appreciated that a function of VGAM726 is inhibition of expression of host target genes, as part of a



novel viral mechanism of attacking a host. Accordingly, utilities of VGAM726 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM726 correlate with, and may be deduced from, the identity of the host target genes which VGAM726 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10129] Nucleotide sequences of the VGAM726 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM726 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM726 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM726 are further described hereinbelow with reference to Table 1.

[10130] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM726 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10131] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 727 (VGAM727) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10132] VGAM727 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM727 was detected is described hereinabove with reference to Figs. 2–8.

[10133] VGAM727 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea enation mosaic virus. VGAM727 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10134] VGAM727 gene, herein designated VGAM GENE, encodes a VGAM727 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM727 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM727 precursor RNA is designated SEQ ID:19718, and is provided hereinbelow with reference to the sequence listing part.

[10135] VGAM727 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM727 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10136] An enzyme complex designated DICER COMPLEX, dices the VGAM727 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM727 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM727 RNA is designated SEQ ID:19719, and is provided hereinbelow with reference to the sequence listing part.

[10137] VGAM727 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM727 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM727 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10138] VGAM727 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM727 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM727 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM727 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM727 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10139] The complementary binding of VGAM727 RNA, herein designated VGAM RNA, to host target binding sites on VGAM727 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM727 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM727 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10140] It is appreciated that VGAM727 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM727 host target genes. The mRNA of each one of this plurality of VGAM727 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM727 RNA, herein designated VGAM

RNA, and which when bound by VGAM727 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM727 host target proteins.

[10141] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM727 gene, herein designated VGAM GENE, on one or more VGAM727 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10142] It is yet further appreciated that a function of VGAM727 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM727 include diagnosis, prevention and treatment of viral infection by Pea enation mosaic virus. Specific functions, and accordingly utilities, of VGAM727 correlate with, and may be deduced from, the identity of the host target genes which VGAM727 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10143] Nucleotide sequences of the VGAM727 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM727 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM727 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM727 are further described hereinbelow with reference to Table 1.

[10144] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM727 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10145] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 728 (VGAM728) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10146] VGAM728 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM728 was detected is described hereinabove with reference to Figs. 2-8.

[10147] VGAM728 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea enation mosaic virus. VGAM728 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10148] VGAM728 gene, herein designated VGAM GENE, encodes a VGAM728 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM728 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM728 precursor RNA is designated SEQ ID:19724, and is provided hereinbelow with reference to the sequence listing part.

[10149] VGAM728 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM728 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10150] An enzyme complex designated DICER COMPLEX, dices the VGAM728 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM728 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM728 RNA is designated SEQ ID:19725, and is provided hereinbelow with reference to the sequence listing part.

[10151] VGAM728 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM728 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM728 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10152] VGAM728 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM728 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM728 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM728 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM728 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10153] The complementary binding of VGAM728 RNA, herein designated VGAM RNA, to host target binding sites on VGAM728 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM728 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM728 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10154] It is appreciated that VGAM728 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM728 host target genes. The mRNA of each one of this plurality of VGAM728 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM728 RNA, herein designated VGAM RNA, and which when bound by VGAM728 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM728 host target proteins.

[10155] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM728 gene, herein designated VGAM GENE, on one or more VGAM728 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10156] It is yet further appreciated that a function of VGAM728 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM728 include diagnosis, prevention and

treatment of viral infection by Pea enation mosaic virus. Specific functions, and accordingly utilities, of VGAM728 correlate with, and may be deduced from, the identity of the host target genes which VGAM728 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10157] Nucleotide sequences of the VGAM728 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM728 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM728 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM728 are further described hereinbelow with reference to Table 1.

[10158] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM728 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10159] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 729 (VGAM729) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10160] VGAM729 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM729 was detected is described hereinabove with reference to Figs. 2–8.

[10161] VGAM729 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM729 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10162] VGAM729 gene, herein designated VGAM GENE, encodes a VGAM729 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM729 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM729 precursor RNA is designated SEQ ID:19750, and is provided hereinbelow with reference to the sequence listing part.

[10163] VGAM729 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM729 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10164] An enzyme complex designated DICER COMPLEX, dices the VGAM729 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM729 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM729 RNA is designated SEQ ID:19751, and is provided hereinbelow with reference to the sequence listing part.

[10165] VGAM729 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM729 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM729 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10166] VGAM729 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM729 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM729 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM729 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM729 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10167] The complementary binding of VGAM729 RNA, herein designated VGAM RNA, to host target binding sites on VGAM729 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM729 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM729 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10168] It is appreciated that VGAM729 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM729 host target genes. The mRNA of each one of this plurality of VGAM729 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM729 RNA, herein designated VGAM RNA, and which when bound by VGAM729 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM729 host target proteins.

[10169] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM729 gene, herein designated VGAM GENE, on one or more VGAM729 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10170] It is yet further appreciated that a function of VGAM729 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM729 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* en-

tomopoxvirus. Specific functions, and accordingly utilities, of VGAM729 correlate with, and may be deduced from, the identity of the host target genes which VGAM729 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10171] Nucleotide sequences of the VGAM729 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM729 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM729 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM729 are further described hereinbelow with reference to Table 1.

[10172] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM729 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10173] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 730 (VGAM730) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[10174] VGAM730 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM730 was detected is described hereinabove with reference to Figs. 2–8.

[10175] VGAM730 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea enation mosaic virus. VGAM730 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10176] VGAM730 gene, herein designated VGAM GENE, encodes a VGAM730 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM730 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM730 precursor RNA is designated SEQ ID:19758, and is provided hereinbelow with reference to the sequence listing part.

[10177] VGAM730 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM730 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10178] An enzyme complex designated DICER COMPLEX, dices the VGAM730 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM730 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM730 RNA is designated SEQ ID:19759, and is provided hereinbelow with reference to the sequence listing part.

[10179] VGAM730 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM730 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM730 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10180] VGAM730 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM730 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM730 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM730 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM730 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10181] The complementary binding of VGAM730 RNA, herein designated VGAM RNA, to host target binding sites on VGAM730 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM730 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM730 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10182] It is appreciated that VGAM730 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM730 host target genes. The mRNA of each one of this plurality of VGAM730 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM730 RNA, herein designated VGAM RNA, and which when bound by VGAM730 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM730 host target proteins.

[10183] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM730 gene, herein designated VGAM GENE, on one or more VGAM730 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10184] It is yet further appreciated that a function of VGAM730 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM730 include diagnosis, prevention and treatment of viral infection by Pea enation mosaic virus. Specific functions, and accordingly utilities, of VGAM730



correlate with, and may be deduced from, the identity of the host target genes which VGAM730 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10185] Nucleotide sequences of the VGAM730 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM730 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM730 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM730 are further described hereinbelow with reference to Table 1.

[10186] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM730 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10187] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 731 (VGAM731) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[10188] VGAM731 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM731 was detected is described hereinabove with reference to Figs. 2–8.

[10189] VGAM731 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea enation mosaic virus. VGAM731 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10190] VGAM731 gene, herein designated VGAM GENE, encodes a VGAM731 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM731 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM731 precursor RNA is designated SEQ ID:19770, and is provided hereinbelow with reference to the sequence listing part.

[10191] VGAM731 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM731 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10192] An enzyme complex designated DICER COMPLEX, dices the VGAM731 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM731 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM731 RNA is designated SEQ ID:19771, and is provided hereinbelow with reference to the sequence listing part.

[10193] VGAM731 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM731 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM731 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10194] VGAM731 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM731 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM731 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM731 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM731 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10195] The complementary binding of VGAM731 RNA, herein designated VGAM RNA, to host target binding sites on VGAM731 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM731 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM731 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10196] It is appreciated that VGAM731 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM731 host target genes. The mRNA of each one of this plurality of VGAM731 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM731 RNA, herein designated VGAM RNA, and which when bound by VGAM731 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM731 host target proteins.

[10197] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM731 gene, herein designated VGAM GENE, on one or more VGAM731 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10198] It is yet further appreciated that a function of VGAM731 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM731 include diagnosis, prevention and treatment of viral infection by Pea enation mosaic virus. Specific functions, and accordingly utilities, of VGAM731 correlate with, and may be deduced from, the identity of

the host target genes which VGAM731 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10199] Nucleotide sequences of the VGAM731 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM731 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM731 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM731 are further described hereinbelow with reference to Table 1.

[10200] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM731 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10201] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 732 (VGAM732) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10202] VGAM732 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM732 was detected is described hereinabove with reference to Figs. 2–8.

[10203] VGAM732 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea enation mosaic virus. VGAM732 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10204] VGAM732 gene, herein designated VGAM GENE, encodes a VGAM732 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM732 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM732 precursor RNA is designated SEQ ID:19842, and is provided hereinbelow with reference to the sequence listing part.

[10205] VGAM732 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM732 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10206] An enzyme complex designated DICER COMPLEX, dices the VGAM732 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM732 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM732 RNA is designated SEQ ID:19843, and is provided hereinbelow with reference to the sequence listing part.

[10207] VGAM732 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM732 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM732 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10208] VGAM732 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM732 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM732 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM732 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM732 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10209] The complementary binding of VGAM732 RNA, herein designated VGAM RNA, to host target binding sites on VGAM732 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM732 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM732 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10210] It is appreciated that VGAM732 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM732 host target genes. The mRNA of each one of this plurality of VGAM732 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM732 RNA, herein designated VGAM RNA, and which when bound by VGAM732 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM732 host target proteins.

[10211] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM732 gene, herein designated VGAM GENE, on one or

more VGAM732 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10212] It is yet further appreciated that a function of VGAM732 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM732 include diagnosis, prevention and treatment of viral infection by Pea enation mosaic virus. Specific functions, and accordingly utilities, of VGAM732 correlate with, and may be deduced from, the identity of the host target genes which VGAM732 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10213] Nucleotide sequences of the VGAM732 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM732 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM732 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM732 are further described hereinbelow with reference to Table 1.

[10214] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM732 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10215] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 733 (VGAM733) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10216] VGAM733 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM733 was detected is described

hereinabove with reference to Figs. 2–8.

[10217] VGAM733 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM733 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10218] VGAM733 gene, herein designated VGAM GENE, encodes a VGAM733 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM733 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM733 precursor RNA is designated SEQ ID:19864, and is provided hereinbelow with reference to the sequence listing part.

[10219] VGAM733 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM733 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10220] An enzyme complex designated DICER COMPLEX, dices the VGAM733 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM733 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM733 RNA is designated SEQ ID:19865, and is provided hereinbelow with reference to the sequence listing part.

[10221] VGAM733 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM733 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM733 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.



[10222] VGAM733 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM733 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM733 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM733 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM733 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10223] The complementary binding of VGAM733 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM733 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM733 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM733 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10224] It is appreciated that VGAM733 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM733 host target genes. The mRNA of each one of this plurality of VGAM733 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM733 RNA, herein designated VGAM RNA, and which when bound by VGAM733 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM733 host target proteins.

[10225] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM733 gene, herein designated VGAM GENE, on one or more VGAM733 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10226] It is yet further appreciated that a function of VGAM733 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM733 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM733 correlate with, and may be deduced from, the identity of the host target genes which VGAM733 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10227] Nucleotide sequences of the VGAM733 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM733 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM733 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM733 are further described hereinbelow with reference to Table 1.

[10228] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM733 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10229] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 734 (VGAM734) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10230] VGAM734 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM734 was detected is described hereinabove with reference to Figs. 2-8.

[10231] VGAM734 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 27. VGAM734 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10232] VGAM734 gene, herein designated VGAM GENE, encodes a VGAM734 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM734 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM734 precursor RNA is designated SEQ ID:19877, and is provided hereinbelow with reference to the sequence listing part.

[10233] VGAM734 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM734 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[10234] An enzyme complex designated DICER COMPLEX, dices the VGAM734 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM734 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM734 RNA is designated SEQ ID:19878, and is provided hereinbelow with reference to the sequence listing part.

[10235] VGAM734 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM734 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM734 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10236] VGAM734 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM734 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM734 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM734 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM734 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10237] The complementary binding of VGAM734 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM734 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM734 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM734 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10238] It is appreciated that VGAM734 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM734 host target genes. The mRNA of each one of this plurality of VGAM734 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM734 RNA, herein designated VGAM RNA, and which when bound by VGAM734 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM734 host target proteins.

[10239] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM734 gene, herein designated VGAM GENE, on one or more VGAM734 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10240] It is yet further appreciated that a function of VGAM734 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM734 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 27. Specific functions, and accordingly utilities, of VGAM734 correlate with, and may be deduced from, the identity of the host target genes which VGAM734 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10241] Nucleotide sequences of the VGAM734 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM734 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM734 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM734 are further described hereinbelow with reference to Table 1.

[10242] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM734 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10243] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 735 (VGAM735) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10244] VGAM735 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM735 was detected is described hereinabove with reference to Figs. 2-8.

[10245] VGAM735 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 4. VGAM735 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10246] VGAM735 gene, herein designated VGAM GENE, encodes a VGAM735 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM735 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM735 precursor RNA is designated SEQ ID:19881, and is provided hereinbelow with reference to the sequence listing part.

[10247] VGAM735 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM735 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10248] An enzyme complex designated DICER COMPLEX, dices the VGAM735 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM735 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM735 RNA is designated SEQ ID:19882, and is provided hereinbelow with reference to the sequence listing part.

[10249] VGAM735 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM735 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM735 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10250] VGAM735 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM735 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM735 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM735 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM735 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10251] The complementary binding of VGAM735 RNA, herein designated VGAM RNA, to host target binding sites on VGAM735 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM735 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM735 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10252] It is appreciated that VGAM735 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM735 host target genes. The mRNA of each one of this plurality of VGAM735 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM735 RNA, herein designated VGAM RNA, and which when bound by VGAM735 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM735 host target proteins.

[10253] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM735 gene, herein designated VGAM GENE, on one or more VGAM735 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10254] It is yet further appreciated that a function of VGAM735 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM735 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM735 correlate with, and may be deduced from, the identity of the host target genes which VGAM735 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10255] Nucleotide sequences of the VGAM735 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM735 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM735 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM735 are further described hereinbelow with reference to Table 1.

[10256] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM735 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10257] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 736 (VGAM736) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10258] VGAM736 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM736 was detected is described hereinabove with reference to Figs. 2-8.

[10259] VGAM736 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious hypodermal



and hematopoietic necrosis virus. VGAM736 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10260] VGAM736 gene, herein designated VGAM GENE, encodes a VGAM736 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM736 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM736 precursor RNA is designated SEQ ID:20056, and is provided hereinbelow with reference to the sequence listing part.

[10261] VGAM736 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM736 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10262] An enzyme complex designated DICER COMPLEX, dices

the VGAM736 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM736 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM736 RNA is designated SEQ ID:20057, and is provided hereinbelow with reference to the sequence listing part.

[10263] VGAM736 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM736 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM736 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10264] VGAM736 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM736 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM736 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM736 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM736 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10265] The complementary binding of VGAM736 RNA, herein designated VGAM RNA, to host target binding sites on VGAM736 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM736 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM736 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10266] It is appreciated that VGAM736 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM736 host target genes. The mRNA of each one of this plurality of VGAM736 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM736 RNA, herein designated VGAM RNA, and which when bound by VGAM736 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM736 host target proteins.

[10267] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM736 gene, herein designated VGAM GENE, on one or more VGAM736 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10268] It is yet further appreciated that a function of VGAM736 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM736 include diagnosis, prevention and treatment of viral infection by Infectious hypodermal and hematopoietic necrosis virus. Specific functions, and accordingly utilities, of VGAM736 correlate with, and may be deduced from, the identity of the host target genes which VGAM736 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10269] Nucleotide sequences of the VGAM736 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM736 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM736 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM736 are further described hereinbelow with reference to Table 1.

[10270] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM736 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10271] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 737 (VGAM737) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10272] VGAM737 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM737 was detected is described hereinabove with reference to Figs. 2-8.

[10273] VGAM737 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious hypodermal and hematopoietic necrosis virus. VGAM737 host target

gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10274] VGAM737 gene, herein designated VGAM GENE, encodes a VGAM737 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM737 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM737 precursor RNA is designated SEQ ID:20065, and is provided hereinbelow with reference to the sequence listing part.

[10275] VGAM737 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM737 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10276] An enzyme complex designated DICER COMPLEX, dices the VGAM737 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM737 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM737 RNA is designated SEQ ID:20066, and is provided hereinbelow with reference to the sequence listing part.

[10277] VGAM737 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM737 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM737 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10278] VGAM737 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM737 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM737 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM737 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM737 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10279] The complementary binding of VGAM737 RNA, herein designated VGAM RNA, to host target binding sites on VGAM737 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM737 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM737 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10280] It is appreciated that VGAM737 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM737 host target genes. The mRNA of each one of this plurality of VGAM737 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM737 RNA, herein designated VGAM RNA, and which when bound by VGAM737 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM737 host target proteins.

[10281] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM737 gene, herein designated VGAM GENE, on one or more VGAM737 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10282] It is yet further appreciated that a function of VGAM737 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM737 include diagnosis, prevention and treatment of viral infection by Infectious hypodermal and hematopoietic necrosis virus. Specific functions, and accordingly utilities, of VGAM737 correlate with, and may be deduced from, the identity of the host target genes which VGAM737 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10283] Nucleotide sequences of the VGAM737 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM737 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM737 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM737 are further described hereinbelow with reference to Table 1.

[10284] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM737 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10285] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 738 (VGAM738) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10286] VGAM738 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM738 was detected is described hereinabove with reference to Figs. 2-8.

[10287] VGAM738 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM738 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[10288] VGAM738 gene, herein designated VGAM GENE, encodes a VGAM738 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM738 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM738 precursor RNA is designated SEQ ID:20082, and is provided hereinbelow with reference to the sequence listing part.

[10289] VGAM738 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM738 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10290] An enzyme complex designated DICER COMPLEX, dices the VGAM738 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM738 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM738 RNA is designated SEQ ID:20083, and is provided hereinbelow with reference to the sequence listing part.

[10291] VGAM738 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM738 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM738 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10292] VGAM738 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM738 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM738 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM738 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM738 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10293] The complementary binding of VGAM738 RNA, herein designated VGAM RNA, to host target binding sites on VGAM738 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM738 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM738 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10294] It is appreciated that VGAM738 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM738 host target genes. The mRNA of each one of this plurality of VGAM738 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM738 RNA, herein designated VGAM RNA, and which when bound by VGAM738 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM738 host target proteins.

[10295] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM738 gene, herein designated VGAM GENE, on one or more VGAM738 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10296] It is yet further appreciated that a function of VGAM738 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM738 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM738 correlate with, and may be deduced from, the identity of the host target genes which VGAM738 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10297] Nucleotide sequences of the VGAM738 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM738 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM738 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM738 are further de-

scribed hereinbelow with reference to Table 1.

[10298] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM738 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10299] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 739 (VGAM739) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10300] VGAM739 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM739 was detected is described hereinabove with reference to Figs. 2-8.

[10301] VGAM739 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM739 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10302] VGAM739 gene, herein designated VGAM GENE, encodes a VGAM739 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM739 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM739 precursor RNA is designated SEQ ID:20099, and is provided hereinbelow with reference to the sequence listing part.

[10303] VGAM739 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM739 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10304] An enzyme complex designated DICER COMPLEX, dices the VGAM739 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM739 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM739 RNA is designated SEQ ID:20100, and is provided hereinbelow with reference to the sequence listing part.

[10305] VGAM739 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM739 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM739 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10306] VGAM739 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM739 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM739 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM739 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM739 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10307] The complementary binding of VGAM739 RNA, herein designated VGAM RNA, to host target binding sites on VGAM739 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM739 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM739 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10308] It is appreciated that VGAM739 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM739 host target genes. The mRNA of each one of this plurality of VGAM739 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM739 RNA, herein designated VGAM RNA, and which when bound by VGAM739 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM739 host target proteins.

[10309] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM739 gene, herein designated VGAM GENE, on one or more VGAM739 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10310] It is yet further appreciated that a function of VGAM739 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM739 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM739 correlate with, and may be deduced from, the identity of the host target genes which VGAM739 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10311] Nucleotide sequences of the VGAM739 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM739 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM739 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM739 are further described hereinbelow with reference to Table 1.

[10312] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM739 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10313] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 740 (VGAM740) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10314] VGAM740 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM740 was detected is described hereinabove with reference to Figs. 2-8.

[10315] VGAM740 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM740 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10316] VGAM740 gene, herein designated VGAM GENE, encodes a



VGAM740 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM740 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM740 precursor RNA is designated SEQ ID:20108, and is provided hereinbelow with reference to the sequence listing part.

[10317] VGAM740 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM740 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10318] An enzyme complex designated DICER COMPLEX, dices the VGAM740 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM740 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM740 RNA is designated SEQ ID:20109, and is provided hereinbelow with reference to the sequence listing part.

[10319] VGAM740 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM740 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM740 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10320] VGAM740 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM740 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM740 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM740 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM740 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10321] The complementary binding of VGAM740 RNA, herein designated VGAM RNA, to host target binding sites on VGAM740 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM740 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM740 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[10322] It is appreciated that VGAM740 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM740 host target genes. The mRNA of each one of this plurality of VGAM740 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM740 RNA, herein designated VGAM RNA, and which when bound by VGAM740 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM740 host target proteins.

[10323] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM740 gene, herein designated VGAM GENE, on one or more VGAM740 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10324] It is yet further appreciated that a function of VGAM740 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM740 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM740 correlate with, and may be deduced from, the identity of the host target genes which VGAM740 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10325] Nucleotide sequences of the VGAM740 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM740 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM740 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM740 are further described hereinbelow with reference to Table 1.

[10326] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM740 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10327] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 741 (VGAM741) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10328] VGAM741 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM741 was detected is described hereinabove with reference to Figs. 2-8.

[10329] VGAM741 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM741 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10330] VGAM741 gene, herein designated VGAM GENE, encodes a VGAM741 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM741 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM741 precursor RNA is designated SEQ ID:20121, and is provided hereinbelow with reference to the sequence listing part.

[10331] VGAM741 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM741 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10332] An enzyme complex designated DICER COMPLEX, dices the VGAM741 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM741 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM741 RNA is designated SEQ ID:20122, and is provided hereinbelow with reference to the sequence listing part.

[10333] VGAM741 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM741 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM741 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10334] VGAM741 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM741 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM741 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host



target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM741 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM741 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10335] The complementary binding of VGAM741 RNA, herein designated VGAM RNA, to host target binding sites on VGAM741 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM741 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM741 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10336] It is appreciated that VGAM741 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM741 host target genes. The mRNA of each one of this plurality of VGAM741 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM741 RNA, herein designated VGAM RNA, and which when bound by VGAM741 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM741 host target proteins.

[10337] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM741 gene, herein designated VGAM GENE, on one or more VGAM741 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10338] It is yet further appreciated that a function of VGAM741 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM741 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM741 correlate with, and may be deduced from, the identity of the host target genes which VGAM741 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10339] Nucleotide sequences of the VGAM741 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM741 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM741 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM741 are further described hereinbelow with reference to Table 1.

[10340] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM741 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10341] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 742 (VGAM742) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10342] VGAM742 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM742 was detected is described hereinabove with reference to Figs. 2–8.

[10343] VGAM742 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM742 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10344] VGAM742 gene, herein designated VGAM GENE, encodes a VGAM742 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM742 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM742 precursor RNA is designated SEQ ID:20128, and is provided hereinbelow with reference to the sequence listing part.

[10345] VGAM742 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM742 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10346] An enzyme complex designated DICER COMPLEX, dices the VGAM742 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM742 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM742 RNA is designated SEQ ID:20129, and is provided hereinbelow with reference to the sequence listing part.

[10347] VGAM742 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM742 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM742 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10348] VGAM742 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM742 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM742 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM742 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM742 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10349] The complementary binding of VGAM742 RNA, herein designated VGAM RNA, to host target binding sites on VGAM742 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM742 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM742 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10350] It is appreciated that VGAM742 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM742 host target genes. The mRNA of each one of this plurality of VGAM742 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM742 RNA, herein designated VGAM RNA, and which when bound by VGAM742 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM742 host target proteins.

[10351] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM742 gene, herein designated VGAM GENE, on one or more VGAM742 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10352] It is yet further appreciated that a function of VGAM742 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM742 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM742 correlate with, and may be deduced from, the identity of the host target genes which VGAM742 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10353] Nucleotide sequences of the VGAM742 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM742 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM742 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM742 are further described hereinbelow with reference to Table 1.

[10354] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM742 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10355] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 743 (VGAM743) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10356] VGAM743 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM743 was detected is described hereinabove with reference to Figs. 2–8.

[10357] VGAM743 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM743 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10358] VGAM743 gene, herein designated VGAM GENE, encodes a VGAM743 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM743 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM743 precursor RNA is designated SEQ ID:20158, and is provided hereinbelow with reference to the sequence listing part.

[10359] VGAM743 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM743 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10360] An enzyme complex designated DICER COMPLEX, dices the VGAM743 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM743 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM743 RNA is designated SEQ ID:20159, and is provided hereinbelow with reference to the sequence listing part.

[10361] VGAM743 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM743 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM743 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10362] VGAM743 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM743 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM743 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM743 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM743 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10363] The complementary binding of VGAM743 RNA, herein designated VGAM RNA, to host target binding sites on VGAM743 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM743 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM743 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10364] It is appreciated that VGAM743 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM743 host target genes. The mRNA of each one of this plurality of VGAM743 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM743 RNA, herein designated VGAM RNA, and which when bound by VGAM743 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM743 host target proteins.

[10365] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM743 gene, herein designated VGAM GENE, on one or more VGAM743 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[10366] It is yet further appreciated that a function of VGAM743 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM743 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM743 correlate with, and may be deduced from, the identity of the host target genes which VGAM743 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10367] Nucleotide sequences of the VGAM743 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM743 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM743 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM743 are further described hereinbelow with reference to Table 1.

[10368] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM743 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10369] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 744 (VGAM744) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10370] VGAM744 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM744 was detected is described hereinabove with reference to Figs. 2–8.

[10371] VGAM744 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM744 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10372] VGAM744 gene, herein designated VGAM GENE, encodes a VGAM744 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM744 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a



protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM744 precursor RNA is designated SEQ ID:20171, and is provided hereinbelow with reference to the sequence listing part.

[10373] VGAM744 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM744 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10374] An enzyme complex designated DICER COMPLEX, dices the VGAM744 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM744 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM744 RNA is designated SEQ ID:20172, and is provided hereinbelow with reference to the sequence listing part.

[10375] VGAM744 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM744 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM744 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10376] VGAM744 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM744 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM744 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM744 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM744 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10377] The complementary binding of VGAM744 RNA, herein designated VGAM RNA, to host target binding sites on VGAM744 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM744 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM744 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10378] It is appreciated that VGAM744 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM744 host target genes. The mRNA of

each one of this plurality of VGAM744 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM744 RNA, herein designated VGAM RNA, and which when bound by VGAM744 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM744 host target proteins.

[10379] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM744 gene, herein designated VGAM GENE, on one or more VGAM744 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[10380] It is yet further appreciated that a function of VGAM744 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM744 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM744 correlate with, and may be deduced from, the identity of the host target genes which VGAM744 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10381] Nucleotide sequences of the VGAM744 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM744 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM744 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM744 are further described hereinbelow with reference to Table 1.

[10382] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM744 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[10383] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 745 (VGAM745) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10384] VGAM745 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM745 was detected is described hereinabove with reference to Figs. 2–8.

[10385] VGAM745 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM745 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10386] VGAM745 gene, herein designated VGAM GENE, encodes a VGAM745 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM745 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM745 precursor RNA is designated SEQ ID:20204, and is provided hereinbelow with reference to the sequence listing part.

[10387] VGAM745 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM745 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10388] An enzyme complex designated DICER COMPLEX, dices the VGAM745 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM745 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM745 RNA is designated SEQ ID:20205, and

is provided hereinbelow with reference to the sequence listing part.

[10389] VGAM745 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM745 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM745 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10390] VGAM745 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM745 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM745 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM745 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM745 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10391] The complementary binding of VGAM745 RNA, herein designated VGAM RNA, to host target binding sites on VGAM745 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM745 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM745 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10392] It is appreciated that VGAM745 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM745 host target genes. The mRNA of each one of this plurality of VGAM745 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM745 RNA, herein designated VGAM RNA, and which when bound by VGAM745 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM745 host target proteins.

[10393] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM745 gene, herein designated VGAM GENE, on one or more VGAM745 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10394] It is yet further appreciated that a function of VGAM745 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM745 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM745 correlate with, and may be deduced from, the identity of the host target genes which VGAM745 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10395] Nucleotide sequences of the VGAM745 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM745 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM745 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM745 are further described hereinbelow with reference to Table 1.

[10396] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM745 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10397] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 746 (VGAM746) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10398] VGAM746 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM746 was detected is described hereinabove with reference to Figs. 2–8.

[10399] VGAM746 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 90. VGAM746 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10400] VGAM746 gene, herein designated VGAM GENE, encodes a VGAM746 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM746 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM746 precursor RNA is

designated SEQ ID:20295, and is provided hereinbelow with reference to the sequence listing part.

[10401] VGAM746 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM746 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10402] An enzyme complex designated DICER COMPLEX, dices the VGAM746 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM746 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM746 RNA is designated SEQ ID:20296, and is provided hereinbelow with reference to the sequence

listing part.

[10403] VGAM746 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM746 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM746 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10404] VGAM746 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM746 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM746 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM746 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM746 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10405] The complementary binding of VGAM746 RNA, herein designated VGAM RNA, to host target binding sites on VGAM746 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM746 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM746 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10406] It is appreciated that VGAM746 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM746 host target genes. The mRNA of each one of this plurality of VGAM746 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM746 RNA, herein designated VGAM RNA, and which when bound by VGAM746 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM746 host target proteins.

[10407] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM746 gene, herein designated VGAM GENE, on one or more VGAM746 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10408] It is yet further appreciated that a function of VGAM746 is



inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM746 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 90. Specific functions, and accordingly utilities, of VGAM746 correlate with, and may be deduced from, the identity of the host target genes which VGAM746 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10409] Nucleotide sequences of the VGAM746 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM746 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM746 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM746 are further described hereinbelow with reference to Table 1.

[10410] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM746 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10411] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 747 (VGAM747) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10412] VGAM747 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM747 was detected is described hereinabove with reference to Figs. 2–8.

[10413] VGAM747 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM747 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10414] VGAM747 gene, herein designated VGAM GENE, encodes a VGAM747 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM747 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM747 precursor RNA is designated SEQ ID:20306, and is provided hereinbelow

with reference to the sequence listing part.

[10415] VGAM747 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM747 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10416] An enzyme complex designated DICER COMPLEX, dices the VGAM747 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM747 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM747 RNA is designated SEQ ID:20307, and is provided hereinbelow with reference to the sequence listing part.

[10417] VGAM747 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM747 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM747 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10418] VGAM747 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM747 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM747 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM747 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM747 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10419] The complementary binding of VGAM747 RNA, herein designated VGAM RNA, to host target binding sites on VGAM747 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM747 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM747 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10420] It is appreciated that VGAM747 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM747 host target genes. The mRNA of each one of this plurality of VGAM747 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM747 RNA, herein designated VGAM RNA, and which when bound by VGAM747 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM747 host target proteins.

[10421] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM747 gene, herein designated VGAM GENE, on one or more VGAM747 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10422] It is yet further appreciated that a function of VGAM747 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM747 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM747 correlate with, and may be deduced from, the identity of the host target genes which VGAM747 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10423] Nucleotide sequences of the VGAM747 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM747 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM747 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM747 are further described hereinbelow with reference to Table 1.

[10424] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM747 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10425] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 748 (VGAM748) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10426] VGAM748 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM748 was detected is described hereinabove with reference to Figs. 2–8.

[10427] VGAM748 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine adenovirus. VGAM748 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10428] VGAM748 gene, herein designated VGAM GENE, encodes a VGAM748 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM748 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM748 precursor RNA is designated SEQ ID:20313, and is provided hereinbelow with reference to the sequence listing part.



[10429] VGAM748 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM748 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10430] An enzyme complex designated DICER COMPLEX, dices the VGAM748 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM748 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM748 RNA is designated SEQ ID:20314, and is provided hereinbelow with reference to the sequence listing part.

[10431] VGAM748 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM748 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM748 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10432] VGAM748 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM748 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM748 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM748 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM748 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10433] The complementary binding of VGAM748 RNA, herein designated VGAM RNA, to host target binding sites on VGAM748 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM748 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM748 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10434] It is appreciated that VGAM748 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM748 host target genes. The mRNA of each one of this plurality of VGAM748 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM748 RNA, herein designated VGAM

RNA, and which when bound by VGAM748 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM748 host target proteins.

[10435] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM748 gene, herein designated VGAM GENE, on one or more VGAM748 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10436] It is yet further appreciated that a function of VGAM748 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM748 include diagnosis, prevention and treatment of viral infection by Canine adenovirus. Specific functions, and accordingly utilities, of VGAM748 correlate with, and may be deduced from, the identity of the host target genes which VGAM748 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10437] Nucleotide sequences of the VGAM748 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM748 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM748 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM748 are further described hereinbelow with reference to Table 1.

[10438] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM748 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10439] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 749 (VGAM749) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10440] VGAM749 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM749 was detected is described hereinabove with reference to Figs. 2-8.

[10441] VGAM749 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine adenovirus. VGAM749 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10442] VGAM749 gene, herein designated VGAM GENE, encodes a VGAM749 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM749 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM749 precursor RNA is designated SEQ ID:20318, and is provided hereinbelow with reference to the sequence listing part.

[10443] VGAM749 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM749 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10444] An enzyme complex designated DICER COMPLEX, dices the VGAM749 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM749 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM749 RNA is designated SEQ ID:20319, and is provided hereinbelow with reference to the sequence listing part.

[10445] VGAM749 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM749 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM749 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10446] VGAM749 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM749 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM749 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM749 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM749 host



target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10447] The complementary binding of VGAM749 RNA, herein designated VGAM RNA, to host target binding sites on VGAM749 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM749 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM749 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10448] It is appreciated that VGAM749 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM749 host target genes. The mRNA of each one of this plurality of VGAM749 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM749 RNA, herein designated VGAM RNA, and which when bound by VGAM749 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM749 host target proteins.

[10449] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM749 gene, herein designated VGAM GENE, on one or more VGAM749 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10450] It is yet further appreciated that a function of VGAM749 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM749 include diagnosis, prevention and

treatment of viral infection by Canine adenovirus. Specific functions, and accordingly utilities, of VGAM749 correlate with, and may be deduced from, the identity of the host target genes which VGAM749 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10451] Nucleotide sequences of the VGAM749 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM749 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM749 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM749 are further described hereinbelow with reference to Table 1.

[10452] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM749 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10453] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 750 (VGAM750) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10454] VGAM750 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM750 was detected is described hereinabove with reference to Figs. 2–8.

[10455] VGAM750 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM750 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10456] VGAM750 gene, herein designated VGAM GENE, encodes a VGAM750 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM750 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM750 precursor RNA is designated SEQ ID:20334, and is provided hereinbelow with reference to the sequence listing part.

[10457] VGAM750 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM750 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10458] An enzyme complex designated DICER COMPLEX, dices the VGAM750 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM750 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM750 RNA is designated SEQ ID:20335, and is provided hereinbelow with reference to the sequence listing part.

[10459] VGAM750 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM750 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM750 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10460] VGAM750 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM750 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM750 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM750 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM750 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10461] The complementary binding of VGAM750 RNA, herein designated VGAM RNA, to host target binding sites on VGAM750 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM750 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM750 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10462] It is appreciated that VGAM750 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM750 host target genes. The mRNA of each one of this plurality of VGAM750 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM750 RNA, herein designated VGAM RNA, and which when bound by VGAM750 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM750 host target proteins.

[10463] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM750 gene, herein designated VGAM GENE, on one or more VGAM750 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10464] It is yet further appreciated that a function of VGAM750 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM750 include diagnosis, prevention and treatment of viral infection by Chimpanzee cy-



tomegalovirus. Specific functions, and accordingly utilities, of VGAM750 correlate with, and may be deduced from, the identity of the host target genes which VGAM750 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10465] Nucleotide sequences of the VGAM750 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM750 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM750 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM750 are further described hereinbelow with reference to Table 1.

[10466] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM750 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10467] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 751 (VGAM751) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[10468] VGAM751 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM751 was detected is described hereinabove with reference to Figs. 2–8.

[10469] VGAM751 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM751 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10470] VGAM751 gene, herein designated VGAM GENE, encodes a VGAM751 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM751 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM751 precursor RNA is designated SEQ ID:20362, and is provided hereinbelow with reference to the sequence listing part.

[10471] VGAM751 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM751 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10472] An enzyme complex designated DICER COMPLEX, dices the VGAM751 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM751 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM751 RNA is designated SEQ ID:20363, and is provided hereinbelow with reference to the sequence listing part.

[10473] VGAM751 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM751 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM751 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10474] VGAM751 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM751 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM751 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM751 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM751 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10475] The complementary binding of VGAM751 RNA, herein designated VGAM RNA, to host target binding sites on VGAM751 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM751 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM751 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10476] It is appreciated that VGAM751 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM751 host target genes. The mRNA of each one of this plurality of VGAM751 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM751 RNA, herein designated VGAM RNA, and which when bound by VGAM751 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM751 host target proteins.

[10477] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM751 gene, herein designated VGAM GENE, on one or more VGAM751 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10478] It is yet further appreciated that a function of VGAM751 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM751 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utili-

ties, of VGAM751 correlate with, and may be deduced from, the identity of the host target genes which VGAM751 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10479] Nucleotide sequences of the VGAM751 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM751 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM751 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM751 are further described hereinbelow with reference to Table 1.

[10480] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM751 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10481] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 752 (VGAM752) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[10482] VGAM752 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM752 was detected is described hereinabove with reference to Figs. 2–8.

[10483] VGAM752 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine adenovirus. VGAM752 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10484] VGAM752 gene, herein designated VGAM GENE, encodes a VGAM752 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM752 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM752 precursor RNA is designated SEQ ID:20487, and is provided hereinbelow with reference to the sequence listing part.

[10485] VGAM752 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM752 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.



As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10486] An enzyme complex designated DICER COMPLEX, dices the VGAM752 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM752 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM752 RNA is designated SEQ ID:20488, and is provided hereinbelow with reference to the sequence listing part.

[10487] VGAM752 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM752 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM752 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10488] VGAM752 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM752 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM752 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM752 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM752 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10489] The complementary binding of VGAM752 RNA, herein designated VGAM RNA, to host target binding sites on VGAM752 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM752 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM752 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10490] It is appreciated that VGAM752 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM752 host target genes. The mRNA of each one of this plurality of VGAM752 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM752 RNA, herein designated VGAM RNA, and which when bound by VGAM752 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM752 host target proteins.

[10491] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM752 gene, herein designated VGAM GENE, on one or more VGAM752 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10492] It is yet further appreciated that a function of VGAM752 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM752 include diagnosis, prevention and treatment of viral infection by Canine adenovirus. Specific functions, and accordingly utilities, of VGAM752 correlate with, and may be deduced from, the identity of the host

target genes which VGAM752 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10493] Nucleotide sequences of the VGAM752 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM752 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM752 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM752 are further described hereinbelow with reference to Table 1.

[10494] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM752 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10495] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 753 (VGAM753) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10496] VGAM753 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM753 was detected is described hereinabove with reference to Figs. 2–8.

[10497] VGAM753 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 90. VGAM753 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10498] VGAM753 gene, herein designated VGAM GENE, encodes a VGAM753 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM753 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM753 precursor RNA is designated SEQ ID:20684, and is provided hereinbelow with reference to the sequence listing part.

[10499] VGAM753 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM753 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10500] An enzyme complex designated DICER COMPLEX, dices the VGAM753 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM753 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM753 RNA is designated SEQ ID:20685, and is provided hereinbelow with reference to the sequence listing part.

[10501] VGAM753 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM753 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM753 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10502] VGAM753 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM753 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM753 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM753 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM753 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-



cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10503] The complementary binding of VGAM753 RNA, herein designated VGAM RNA, to host target binding sites on VGAM753 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM753 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM753 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10504] It is appreciated that VGAM753 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM753 host target genes. The mRNA of each one of this plurality of VGAM753 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM753 RNA, herein designated VGAM RNA, and which when bound by VGAM753 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM753 host target proteins.

[10505] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM753 gene, herein designated VGAM GENE, on one or more VGAM753 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10506] It is yet further appreciated that a function of VGAM753 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM753 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 90. Specific functions, and accordingly utilities, of VGAM753 correlate with, and may be deduced from, the identity of the host target genes which VGAM753 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10507] Nucleotide sequences of the VGAM753 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM753 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM753 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM753 are further described hereinbelow with reference to Table 1.

[10508] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM753 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10509] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 754 (VGAM754) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10510] VGAM754 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM754 was detected is described hereinabove with reference to Figs. 2–8.

[10511] VGAM754 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM754 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10512] VGAM754 gene, herein designated VGAM GENE, encodes a VGAM754 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM754 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM754 precursor RNA is designated SEQ ID:20709, and is provided hereinbelow with reference to the sequence listing part.

[10513] VGAM754 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM754 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10514] An enzyme complex designated DICER COMPLEX, dices the VGAM754 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM754 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM754 RNA is designated SEQ ID:20710, and is provided hereinbelow with reference to the sequence listing part.

[10515] VGAM754 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM754 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM754 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10516] VGAM754 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM754 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM754 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM754 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM754 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[10517] The complementary binding of VGAM754 RNA, herein designated VGAM RNA, to host target binding sites on VGAM754 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM754 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM754 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10518] It is appreciated that VGAM754 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM754 host target genes. The mRNA of each one of this plurality of VGAM754 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM754 RNA, herein designated VGAM RNA, and which when bound by VGAM754 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM754 host target proteins.

[10519] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM754 gene, herein designated VGAM GENE, on one or more VGAM754 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10520] It is yet further appreciated that a function of VGAM754 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM754 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM754 correlate with, and may be deduced from, the identity of the host target genes which VGAM754 binds and inhibits, and the function of these



host target genes, as elaborated hereinbelow.

[10521] Nucleotide sequences of the VGAM754 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM754 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM754 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM754 are further described hereinbelow with reference to Table 1.

[10522] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM754 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10523] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 755 (VGAM755) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10524] VGAM755 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM755 was detected is described hereinabove with reference to Figs. 2–8.

[10525] VGAM755 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 90. VGAM755 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10526] VGAM755 gene, herein designated VGAM GENE, encodes a VGAM755 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM755 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM755 precursor RNA is designated SEQ ID:20724, and is provided hereinbelow with reference to the sequence listing part.

[10527] VGAM755 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM755 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10528] An enzyme complex designated DICER COMPLEX, dices the VGAM755 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM755 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM755 RNA is designated SEQ ID:20725, and is provided hereinbelow with reference to the sequence listing part.

[10529] VGAM755 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM755 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM755 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[10530] VGAM755 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM755 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM755 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM755 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM755 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10531] The complementary binding of VGAM755 RNA, herein designated VGAM RNA, to host target binding sites on VGAM755 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM755 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM755 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10532] It is appreciated that VGAM755 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM755 host target genes. The mRNA of each one of this plurality of VGAM755 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM755 RNA, herein designated VGAM RNA, and which when bound by VGAM755 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM755 host target proteins.

[10533] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM755 gene, herein designated VGAM GENE, on one or

more VGAM755 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10534] It is yet further appreciated that a function of VGAM755 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM755 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 90. Specific functions, and accordingly utilities, of VGAM755 correlate with, and may be deduced from, the identity of the host target genes which VGAM755 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10535] Nucleotide sequences of the VGAM755 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM755 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM755 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM755 are further described hereinbelow with reference to Table 1.

[10536] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM755 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10537] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 756 (VGAM756) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10538] VGAM756 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM756 was detected is described

hereinabove with reference to Figs. 2–8.

[10539] VGAM756 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM756 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10540] VGAM756 gene, herein designated VGAM GENE, encodes a VGAM756 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM756 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM756 precursor RNA is designated SEQ ID:20735, and is provided hereinbelow with reference to the sequence listing part.

[10541] VGAM756 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM756 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10542] An enzyme complex designated DICER COMPLEX, dices the VGAM756 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM756 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM756 RNA is designated SEQ ID:20736, and is provided hereinbelow with reference to the sequence listing part.

[10543] VGAM756 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM756 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM756 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10544] VGAM756 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM756 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM756 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM756 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM756 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10545] The complementary binding of VGAM756 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM756 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM756 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM756 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10546] It is appreciated that VGAM756 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM756 host target genes. The mRNA of each one of this plurality of VGAM756 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM756 RNA, herein designated VGAM RNA, and which when bound by VGAM756 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM756 host target proteins.

[10547] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM756 gene, herein designated VGAM GENE, on one or more VGAM756 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10548] It is yet further appreciated that a function of VGAM756 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM756 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM756 correlate with, and may be deduced from, the identity of the host target genes which VGAM756 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10549] Nucleotide sequences of the VGAM756 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM756 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM756 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM756 are further described hereinbelow with reference to Table 1.

[10550] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM756 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10551] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 757 (VGAM757) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10552] VGAM757 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM757 was detected is described hereinabove with reference to Figs. 2-8.

[10553] VGAM757 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM757 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10554] VGAM757 gene, herein designated VGAM GENE, encodes a VGAM757 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM757 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM757 precursor RNA is designated SEQ ID:20746, and is provided hereinbelow with reference to the sequence listing part.

[10555] VGAM757 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM757 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[10556] An enzyme complex designated DICER COMPLEX, dices the VGAM757 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM757 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM757 RNA is designated SEQ ID:20747, and is provided hereinbelow with reference to the sequence listing part.

[10557] VGAM757 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM757 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM757 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10558] VGAM757 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM757 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM757 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM757 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM757 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10559] The complementary binding of VGAM757 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM757 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM757 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM757 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10560] It is appreciated that VGAM757 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM757 host target genes. The mRNA of each one of this plurality of VGAM757 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM757 RNA, herein designated VGAM RNA, and which when bound by VGAM757 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM757 host target proteins.

[10561] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM757 gene, herein designated VGAM GENE, on one or more VGAM757 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10562] It is yet further appreciated that a function of VGAM757 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM757 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM757 correlate with, and may be deduced from, the identity of the host target genes which VGAM757 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10563] Nucleotide sequences of the VGAM757 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM757 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM757 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM757 are further described hereinbelow with reference to Table 1.

[10564] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM757 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10565] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 758 (VGAM758) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10566] VGAM758 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM758 was detected is described hereinabove with reference to Figs. 2-8.

[10567] VGAM758 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM758 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10568] VGAM758 gene, herein designated VGAM GENE, encodes a VGAM758 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM758 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM758 precursor RNA is designated SEQ ID:20790, and is provided hereinbelow with reference to the sequence listing part.

[10569] VGAM758 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM758 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10570] An enzyme complex designated DICER COMPLEX, dices the VGAM758 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM758 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM758 RNA is designated SEQ ID:20791, and is provided hereinbelow with reference to the sequence listing part.

[10571] VGAM758 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM758 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM758 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10572] VGAM758 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM758 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM758 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM758 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM758 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10573] The complementary binding of VGAM758 RNA, herein designated VGAM RNA, to host target binding sites on VGAM758 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM758 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM758 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10574] It is appreciated that VGAM758 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM758 host target genes. The mRNA of each one of this plurality of VGAM758 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM758 RNA, herein designated VGAM RNA, and which when bound by VGAM758 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM758 host target proteins.

[10575] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM758 gene, herein designated VGAM GENE, on one or more VGAM758 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10576] It is yet further appreciated that a function of VGAM758 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM758 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM758 correlate with, and may be deduced from, the identity of the host target genes which VGAM758 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10577] Nucleotide sequences of the VGAM758 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM758 RNA, herein designated VGAM RNA, and a



schematic representation of the secondary folding of VGAM758 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM758 are further described hereinbelow with reference to Table 1.

[10578] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM758 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10579] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 759 (VGAM759) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10580] VGAM759 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM759 was detected is described hereinabove with reference to Figs. 2-8.

[10581] VGAM759 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and

kidney necrosis virus. VGAM759 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10582] VGAM759 gene, herein designated VGAM GENE, encodes a VGAM759 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM759 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM759 precursor RNA is designated SEQ ID:20796, and is provided hereinbelow with reference to the sequence listing part.

[10583] VGAM759 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM759 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10584] An enzyme complex designated DICER COMPLEX, dices

the VGAM759 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM759 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM759 RNA is designated SEQ ID:20797, and is provided hereinbelow with reference to the sequence listing part.

[10585] VGAM759 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM759 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM759 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10586] VGAM759 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM759 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM759 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM759 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM759 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10587] The complementary binding of VGAM759 RNA, herein designated VGAM RNA, to host target binding sites on VGAM759 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM759 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM759 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10588] It is appreciated that VGAM759 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM759 host target genes. The mRNA of each one of this plurality of VGAM759 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM759 RNA, herein designated VGAM RNA, and which when bound by VGAM759 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM759 host target proteins.

[10589] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM759 gene, herein designated VGAM GENE, on one or more VGAM759 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10590] It is yet further appreciated that a function of VGAM759 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM759 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM759 correlate with, and may be deduced from, the identity of the host target genes which VGAM759 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10591] Nucleotide sequences of the VGAM759 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM759 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM759 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM759 are further described hereinbelow with reference to Table 1.

[10592] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM759 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10593] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 760 (VGAM760) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10594] VGAM760 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM760 was detected is described hereinabove with reference to Figs. 2-8.

[10595] VGAM760 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM760 host target gene, herein

designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10596] VGAM760 gene, herein designated VGAM GENE, encodes a VGAM760 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM760 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM760 precursor RNA is designated SEQ ID:20823, and is provided hereinbelow with reference to the sequence listing part.

[10597] VGAM760 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM760 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10598] An enzyme complex designated DICER COMPLEX, dices the VGAM760 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM760 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM760 RNA is designated SEQ ID:20824, and is provided hereinbelow with reference to the sequence listing part.

[10599] VGAM760 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM760 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM760 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10600] VGAM760 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM760 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM760 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM760 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM760 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10601] The complementary binding of VGAM760 RNA, herein designated VGAM RNA, to host target binding sites on VGAM760 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM760 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM760 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10602] It is appreciated that VGAM760 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM760 host target genes. The mRNA of each one of this plurality of VGAM760 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM760 RNA, herein designated VGAM RNA, and which when bound by VGAM760 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM760 host target proteins.

[10603] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM760 gene, herein designated VGAM GENE, on one or more VGAM760 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10604] It is yet further appreciated that a function of VGAM760 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM760 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM760 correlate with, and may be deduced from, the identity of the host target genes which VGAM760 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10605] Nucleotide sequences of the VGAM760 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM760 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM760 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM760 are further described hereinbelow with reference to Table 1.

[10606] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM760 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10607] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 761 (VGAM761) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10608] VGAM761 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM761 was detected is described hereinabove with reference to Figs. 2-8.

[10609] VGAM761 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious spleen and kidney necrosis virus. VGAM761 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene

contained in the human genome.

[10610] VGAM761 gene, herein designated VGAM GENE, encodes a VGAM761 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM761 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM761 precursor RNA is designated SEQ ID:20832, and is provided hereinbelow with reference to the sequence listing part.

[10611] VGAM761 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM761 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10612] An enzyme complex designated DICER COMPLEX, dices the VGAM761 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM761 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM761 RNA is designated SEQ ID:20833, and is provided hereinbelow with reference to the sequence listing part.

[10613] VGAM761 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM761 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM761 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10614] VGAM761 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM761 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM761 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM761 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM761 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10615] The complementary binding of VGAM761 RNA, herein designated VGAM RNA, to host target binding sites on VGAM761 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM761 host target RNA, herein designated VGAM HOST TARGET RNA,



into VGAM761 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10616] It is appreciated that VGAM761 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM761 host target genes. The mRNA of each one of this plurality of VGAM761 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM761 RNA, herein designated VGAM RNA, and which when bound by VGAM761 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM761 host target proteins.

[10617] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM761 gene, herein designated VGAM GENE, on one or more VGAM761 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10618] It is yet further appreciated that a function of VGAM761 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM761 include diagnosis, prevention and treatment of viral infection by Infectious spleen and kidney necrosis virus. Specific functions, and accordingly utilities, of VGAM761 correlate with, and may be deduced from, the identity of the host target genes which VGAM761 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10619] Nucleotide sequences of the VGAM761 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM761 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM761 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM761 are further de-

scribed hereinbelow with reference to Table 1.

[10620] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM761 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10621] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 762 (VGAM762) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10622] VGAM762 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM762 was detected is described hereinabove with reference to Figs. 2-8.

[10623] VGAM762 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM762 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10624] VGAM762 gene, herein designated VGAM GENE, encodes a VGAM762 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM762 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM762 precursor RNA is designated SEQ ID:20857, and is provided hereinbelow with reference to the sequence listing part.

[10625] VGAM762 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM762 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10626] An enzyme complex designated DICER COMPLEX, dices the VGAM762 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM762 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM762 RNA is designated SEQ ID:20858, and is provided hereinbelow with reference to the sequence listing part.

[10627] VGAM762 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM762 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM762 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10628] VGAM762 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM762 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM762 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM762 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM762 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10629] The complementary binding of VGAM762 RNA, herein designated VGAM RNA, to host target binding sites on VGAM762 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM762 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM762 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10630] It is appreciated that VGAM762 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM762 host target genes. The mRNA of each one of this plurality of VGAM762 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM762 RNA, herein designated VGAM RNA, and which when bound by VGAM762 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM762 host target proteins.

[10631] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM762 gene, herein designated VGAM GENE, on one or more VGAM762 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10632] It is yet further appreciated that a function of VGAM762 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM762 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM762 correlate with, and may be deduced from, the identity of the host target genes which VGAM762 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10633] Nucleotide sequences of the VGAM762 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM762 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM762 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM762 are further described hereinbelow with reference to Table 1.



[10634] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM762 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10635] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 763 (VGAM763) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10636] VGAM763 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM763 was detected is described hereinabove with reference to Figs. 2-8.

[10637] VGAM763 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM763 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10638] VGAM763 gene, herein designated VGAM GENE, encodes a

VGAM763 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM763 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM763 precursor RNA is designated SEQ ID:20869, and is provided hereinbelow with reference to the sequence listing part.

[10639] VGAM763 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM763 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10640] An enzyme complex designated DICER COMPLEX, dices the VGAM763 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM763 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM763 RNA is designated SEQ ID:20870, and is provided hereinbelow with reference to the sequence listing part.

[10641] VGAM763 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM763 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM763 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10642] VGAM763 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM763 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM763 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM763 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM763 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10643] The complementary binding of VGAM763 RNA, herein designated VGAM RNA, to host target binding sites on VGAM763 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM763 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM763 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[10644] It is appreciated that VGAM763 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM763 host target genes. The mRNA of each one of this plurality of VGAM763 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM763 RNA, herein designated VGAM RNA, and which when bound by VGAM763 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM763 host target proteins.

[10645] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM763 gene, herein designated VGAM GENE, on one or more VGAM763 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10646] It is yet further appreciated that a function of VGAM763 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM763 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM763 correlate with, and may be deduced from, the identity of the host target genes which VGAM763 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10647] Nucleotide sequences of the VGAM763 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM763 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM763 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM763 are further described hereinbelow with reference to Table 1.

[10648] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM763 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10649] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 764 (VGAM764) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10650] VGAM764 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM764 was detected is described hereinabove with reference to Figs. 2-8.

[10651] VGAM764 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine rhinovirus 3. VGAM764 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10652] VGAM764 gene, herein designated VGAM GENE, encodes a VGAM764 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM764 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM764 precursor RNA is designated SEQ ID:20886, and is provided hereinbelow with reference to the sequence listing part.

[10653] VGAM764 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM764 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10654] An enzyme complex designated DICER COMPLEX, dices the VGAM764 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM764 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM764 RNA is designated SEQ ID:20887, and is provided hereinbelow with reference to the sequence listing part.

[10655] VGAM764 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM764 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM764 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10656] VGAM764 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM764 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM764 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM764 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM764 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10657] The complementary binding of VGAM764 RNA, herein designated VGAM RNA, to host target binding sites on VGAM764 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM764 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM764 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10658] It is appreciated that VGAM764 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM764 host target genes. The mRNA of each one of this plurality of VGAM764 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM764 RNA, herein designated VGAM RNA, and which when bound by VGAM764 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM764 host target proteins.

[10659] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM764 gene, herein designated VGAM GENE, on one or more VGAM764 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10660] It is yet further appreciated that a function of VGAM764 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM764 include diagnosis, prevention and treatment of viral infection by Equine rhinovirus 3. Specific functions, and accordingly utilities, of VGAM764 correlate with, and may be deduced from, the identity of the host target genes which VGAM764 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10661] Nucleotide sequences of the VGAM764 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM764 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM764 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM764 are further described hereinbelow with reference to Table 1.

[10662] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM764 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10663] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 765 (VGAM765) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10664] VGAM765 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM765 was detected is described hereinabove with reference to Figs. 2–8.

[10665] VGAM765 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine rhinovirus 3. VGAM765 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10666] VGAM765 gene, herein designated VGAM GENE, encodes a VGAM765 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM765 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM765 precursor RNA is designated SEQ ID:20912, and is provided hereinbelow with reference to the sequence listing part.

[10667] VGAM765 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM765 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10668] An enzyme complex designated DICER COMPLEX, dices the VGAM765 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM765 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM765 RNA is designated SEQ ID:20913, and is provided hereinbelow with reference to the sequence listing part.

[10669] VGAM765 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM765 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM765 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10670] VGAM765 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM765 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM765 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM765 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM765 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10671] The complementary binding of VGAM765 RNA, herein designated VGAM RNA, to host target binding sites on VGAM765 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM765 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM765 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10672] It is appreciated that VGAM765 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM765 host target genes. The mRNA of each one of this plurality of VGAM765 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM765 RNA, herein designated VGAM RNA, and which when bound by VGAM765 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM765 host target proteins.

[10673] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM765 gene, herein designated VGAM GENE, on one or more VGAM765 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10674] It is yet further appreciated that a function of VGAM765 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM765 include diagnosis, prevention and treatment of viral infection by Equine rhinovirus 3. Specific functions, and accordingly utilities, of VGAM765 correlate with, and may be deduced from, the identity of the host target genes which VGAM765 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10675] Nucleotide sequences of the VGAM765 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM765 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM765 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM765 are further described hereinbelow with reference to Table 1.

[10676] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM765 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10677] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 766 (VGAM766) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10678] VGAM766 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM766 was detected is described hereinabove with reference to Figs. 2–8.

[10679] VGAM766 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM766 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10680] VGAM766 gene, herein designated VGAM GENE, encodes a VGAM766 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM766 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM766 precursor RNA is designated SEQ ID:20920, and is provided hereinbelow with reference to the sequence listing part.

[10681] VGAM766 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM766 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10682] An enzyme complex designated DICER COMPLEX, dices the VGAM766 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM766 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 55%) nucleotide sequence of VGAM766 RNA is designated SEQ ID:20921, and is provided hereinbelow with reference to the sequence listing part.

[10683] VGAM766 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM766 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM766 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10684] VGAM766 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM766 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM766 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM766 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM766 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10685] The complementary binding of VGAM766 RNA, herein designated VGAM RNA, to host target binding sites on VGAM766 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM766 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM766 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10686] It is appreciated that VGAM766 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM766 host target genes. The mRNA of each one of this plurality of VGAM766 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM766 RNA, herein designated VGAM RNA, and which when bound by VGAM766 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM766 host target proteins.

[10687] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM766 gene, herein designated VGAM GENE, on one or more VGAM766 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[10688] It is yet further appreciated that a function of VGAM766 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM766 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM766 correlate with, and may be deduced from, the identity of the host target genes which VGAM766 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10689] Nucleotide sequences of the VGAM766 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM766 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM766 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM766 are further described hereinbelow with reference to Table 1.

[10690] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM766 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10691] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 767 (VGAM767) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10692] VGAM767 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM767 was detected is described hereinabove with reference to Figs. 2–8.

[10693] VGAM767 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM767 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10694] VGAM767 gene, herein designated VGAM GENE, encodes a VGAM767 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM767 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM767 precursor RNA is designated SEQ ID:20935, and is provided hereinbelow with reference to the sequence listing part.

[10695] VGAM767 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM767 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10696] An enzyme complex designated DICER COMPLEX, dices the VGAM767 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM767 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM767 RNA is designated SEQ ID:20936, and is provided hereinbelow with reference to the sequence listing part.

[10697] VGAM767 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM767 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM767 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10698] VGAM767 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM767 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM767 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM767 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM767 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10699] The complementary binding of VGAM767 RNA, herein designated VGAM RNA, to host target binding sites on VGAM767 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM767 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM767 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10700] It is appreciated that VGAM767 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM767 host target genes. The mRNA of

each one of this plurality of VGAM767 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM767 RNA, herein designated VGAM RNA, and which when bound by VGAM767 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM767 host target proteins.

[10701] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM767 gene, herein designated VGAM GENE, on one or more VGAM767 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[10702] It is yet further appreciated that a function of VGAM767 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM767 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM767 correlate with, and may be deduced from, the identity of the host target genes which VGAM767 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10703] Nucleotide sequences of the VGAM767 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM767 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM767 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM767 are further described hereinbelow with reference to Table 1.

[10704] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM767 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[10705] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 768 (VGAM768) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10706] VGAM768 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM768 was detected is described hereinabove with reference to Figs. 2–8.

[10707] VGAM768 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM768 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10708] VGAM768 gene, herein designated VGAM GENE, encodes a VGAM768 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM768 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM768 precursor RNA is designated SEQ ID:20950, and is provided hereinbelow with reference to the sequence listing part.

[10709] VGAM768 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM768 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10710] An enzyme complex designated DICER COMPLEX, dices the VGAM768 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM768 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM768 RNA is designated SEQ ID:20951, and



is provided hereinbelow with reference to the sequence listing part.

[10711] VGAM768 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM768 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM768 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10712] VGAM768 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM768 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM768 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM768 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM768 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10713] The complementary binding of VGAM768 RNA, herein designated VGAM RNA, to host target binding sites on VGAM768 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM768 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM768 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10714] It is appreciated that VGAM768 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM768 host target genes. The mRNA of each one of this plurality of VGAM768 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM768 RNA, herein designated VGAM RNA, and which when bound by VGAM768 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM768 host target proteins.

[10715] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM768 gene, herein designated VGAM GENE, on one or more VGAM768 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10716] It is yet further appreciated that a function of VGAM768 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM768 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM768 correlate with, and may be deduced from, the identity of the host target genes which VGAM768 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10717] Nucleotide sequences of the VGAM768 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM768 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM768 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM768 are further described hereinbelow with reference to Table 1.

[10718] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM768 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10719] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 769 (VGAM769) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10720] VGAM769 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM769 was detected is described hereinabove with reference to Figs. 2–8.

[10721] VGAM769 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine immunodeficiency virus. VGAM769 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10722] VGAM769 gene, herein designated VGAM GENE, encodes a VGAM769 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM769 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM769 precursor RNA is

designated SEQ ID:20969, and is provided hereinbelow with reference to the sequence listing part.

[10723] VGAM769 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM769 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10724] An enzyme complex designated DICER COMPLEX, dices the VGAM769 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM769 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM769 RNA is designated SEQ ID:20970, and is provided hereinbelow with reference to the sequence

listing part.

[10725] VGAM769 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM769 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM769 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10726] VGAM769 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM769 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM769 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM769 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM769 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10727] The complementary binding of VGAM769 RNA, herein designated VGAM RNA, to host target binding sites on VGAM769 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM769 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM769 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10728] It is appreciated that VGAM769 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM769 host target genes. The mRNA of each one of this plurality of VGAM769 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM769 RNA, herein designated VGAM RNA, and which when bound by VGAM769 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM769 host target proteins.

[10729] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM769 gene, herein designated VGAM GENE, on one or more VGAM769 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10730] It is yet further appreciated that a function of VGAM769 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM769 include diagnosis, prevention and treatment of viral infection by Bovine immunodeficiency virus. Specific functions, and accordingly utilities, of VGAM769 correlate with, and may be deduced from, the identity of the host target genes which VGAM769 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10731] Nucleotide sequences of the VGAM769 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM769 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM769 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM769 are further described hereinbelow with reference to Table 1.

[10732] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM769 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10733] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 770 (VGAM770) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10734] VGAM770 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM770 was detected is described hereinabove with reference to Figs. 2–8.

[10735] VGAM770 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine immunodeficiency virus. VGAM770 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10736] VGAM770 gene, herein designated VGAM GENE, encodes a VGAM770 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM770 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM770 precursor RNA is designated SEQ ID:21074, and is provided hereinbelow

with reference to the sequence listing part.

[10737] VGAM770 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM770 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10738] An enzyme complex designated DICER COMPLEX, dices the VGAM770 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM770 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM770 RNA is designated SEQ ID:21075, and is provided hereinbelow with reference to the sequence listing part.

[10739] VGAM770 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM770 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM770 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10740] VGAM770 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM770 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM770 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM770 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM770 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10741] The complementary binding of VGAM770 RNA, herein designated VGAM RNA, to host target binding sites on VGAM770 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM770 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM770 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10742] It is appreciated that VGAM770 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM770 host target genes. The mRNA of each one of this plurality of VGAM770 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM770 RNA, herein designated VGAM RNA, and which when bound by VGAM770 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM770 host target proteins.

[10743] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM770 gene, herein designated VGAM GENE, on one or more VGAM770 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10744] It is yet further appreciated that a function of VGAM770 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM770 include diagnosis, prevention and treatment of viral infection by Bovine immunodeficiency virus. Specific functions, and accordingly utilities, of VGAM770 correlate with, and may be deduced from, the identity of the host target genes which VGAM770 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10745] Nucleotide sequences of the VGAM770 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM770 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM770 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM770 are further described hereinbelow with reference to Table 1.

[10746] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM770 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10747] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 771 (VGAM771) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10748] VGAM771 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM771 was detected is described hereinabove with reference to Figs. 2–8.

[10749] VGAM771 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus D. VGAM771 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10750] VGAM771 gene, herein designated VGAM GENE, encodes a VGAM771 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM771 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM771 precursor RNA is designated SEQ ID:21094, and is provided hereinbelow with reference to the sequence listing part.

[10751] VGAM771 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM771 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10752] An enzyme complex designated DICER COMPLEX, dices the VGAM771 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM771 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM771 RNA is designated SEQ ID:21095, and is provided hereinbelow with reference to the sequence listing part.

[10753] VGAM771 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM771 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM771 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10754] VGAM771 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM771 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM771 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM771 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM771 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10755] The complementary binding of VGAM771 RNA, herein designated VGAM RNA, to host target binding sites on VGAM771 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM771 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM771 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10756] It is appreciated that VGAM771 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM771 host target genes. The mRNA of each one of this plurality of VGAM771 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM771 RNA, herein designated VGAM

RNA, and which when bound by VGAM771 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM771 host target proteins.

[10757] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM771 gene, herein designated VGAM GENE, on one or more VGAM771 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10758] It is yet further appreciated that a function of VGAM771 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM771 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus D. Specific functions, and accordingly utilities, of VGAM771 correlate with, and may be deduced from, the identity of the host target genes which VGAM771 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10759] Nucleotide sequences of the VGAM771 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM771 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM771 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM771 are further described hereinbelow with reference to Table 1.

[10760] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM771 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10761] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 772 (VGAM772) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10762] VGAM772 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM772 was detected is described hereinabove with reference to Figs. 2-8.

[10763] VGAM772 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine immunodeficiency virus. VGAM772 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10764] VGAM772 gene, herein designated VGAM GENE, encodes a VGAM772 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM772 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM772 precursor RNA is designated SEQ ID:21106, and is provided hereinbelow with reference to the sequence listing part.

[10765] VGAM772 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM772 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10766] An enzyme complex designated DICER COMPLEX, dices the VGAM772 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM772 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM772 RNA is designated SEQ ID:21107, and is provided hereinbelow with reference to the sequence listing part.

[10767] VGAM772 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM772 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM772 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10768] VGAM772 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM772 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM772 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM772 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM772 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10769] The complementary binding of VGAM772 RNA, herein designated VGAM RNA, to host target binding sites on VGAM772 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM772 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM772 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10770] It is appreciated that VGAM772 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM772 host target genes. The mRNA of each one of this plurality of VGAM772 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM772 RNA, herein designated VGAM RNA, and which when bound by VGAM772 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM772 host target proteins.

[10771] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM772 gene, herein designated VGAM GENE, on one or more VGAM772 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10772] It is yet further appreciated that a function of VGAM772 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM772 include diagnosis, prevention and

treatment of viral infection by Bovine immunodeficiency virus. Specific functions, and accordingly utilities, of VGAM772 correlate with, and may be deduced from, the identity of the host target genes which VGAM772 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10773] Nucleotide sequences of the VGAM772 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM772 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM772 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM772 are further described hereinbelow with reference to Table 1.

[10774] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM772 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10775] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 773 (VGAM773) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10776] VGAM773 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM773 was detected is described hereinabove with reference to Figs. 2–8.

[10777] VGAM773 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM773 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10778] VGAM773 gene, herein designated VGAM GENE, encodes a VGAM773 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM773 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM773 precursor RNA is designated SEQ ID:21115, and is provided hereinbelow with reference to the sequence listing part.

[10779] VGAM773 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM773 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10780] An enzyme complex designated DICER COMPLEX, dices the VGAM773 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM773 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM773 RNA is designated SEQ ID:21116, and is provided hereinbelow with reference to the sequence listing part.

[10781] VGAM773 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM773 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM773 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10782] VGAM773 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM773 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM773 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM773 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM773 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10783] The complementary binding of VGAM773 RNA, herein designated VGAM RNA, to host target binding sites on VGAM773 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM773 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM773 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10784] It is appreciated that VGAM773 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM773 host target genes. The mRNA of each one of this plurality of VGAM773 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM773 RNA, herein designated VGAM RNA, and which when bound by VGAM773 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM773 host target proteins.

[10785] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM773 gene, herein designated VGAM GENE, on one or more VGAM773 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10786] It is yet further appreciated that a function of VGAM773 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM773 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadi-

novirus. Specific functions, and accordingly utilities, of VGAM773 correlate with, and may be deduced from, the identity of the host target genes which VGAM773 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10787] Nucleotide sequences of the VGAM773 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM773 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM773 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM773 are further described hereinbelow with reference to Table 1.

[10788] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM773 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10789] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 774 (VGAM774) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[10790] VGAM774 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM774 was detected is described hereinabove with reference to Figs. 2–8.

[10791] VGAM774 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM774 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10792] VGAM774 gene, herein designated VGAM GENE, encodes a VGAM774 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM774 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM774 precursor RNA is designated SEQ ID:21118, and is provided hereinbelow with reference to the sequence listing part.

[10793] VGAM774 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM774 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10794] An enzyme complex designated DICER COMPLEX, dices the VGAM774 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM774 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM774 RNA is designated SEQ ID:21119, and is provided hereinbelow with reference to the sequence listing part.

[10795] VGAM774 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM774 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM774 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10796] VGAM774 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM774 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM774 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM774 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM774 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10797] The complementary binding of VGAM774 RNA, herein designated VGAM RNA, to host target binding sites on VGAM774 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM774 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM774 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10798] It is appreciated that VGAM774 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM774 host target genes. The mRNA of each one of this plurality of VGAM774 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM774 RNA, herein designated VGAM RNA, and which when bound by VGAM774 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM774 host target proteins.

[10799] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM774 gene, herein designated VGAM GENE, on one or more VGAM774 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10800] It is yet further appreciated that a function of VGAM774 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM774 include diagnosis, prevention and treatment of viral infection by Macaca mulatta rhadinovirus. Specific functions, and accordingly utilities, of

VGAM774 correlate with, and may be deduced from, the identity of the host target genes which VGAM774 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10801] Nucleotide sequences of the VGAM774 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM774 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM774 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM774 are further described hereinbelow with reference to Table 1.

[10802] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM774 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10803] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 775 (VGAM775) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[10804] VGAM775 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM775 was detected is described hereinabove with reference to Figs. 2–8.

[10805] VGAM775 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM775 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10806] VGAM775 gene, herein designated VGAM GENE, encodes a VGAM775 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM775 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM775 precursor RNA is designated SEQ ID:21123, and is provided hereinbelow with reference to the sequence listing part.

[10807] VGAM775 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM775 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10808] An enzyme complex designated DICER COMPLEX, dices the VGAM775 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM775 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM775 RNA is designated SEQ ID:21124, and is provided hereinbelow with reference to the sequence listing part.

[10809] VGAM775 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM775 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM775 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10810] VGAM775 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM775 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM775 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM775 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM775 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10811] The complementary binding of VGAM775 RNA, herein designated VGAM RNA, to host target binding sites on VGAM775 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM775 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM775 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10812] It is appreciated that VGAM775 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM775 host target genes. The mRNA of each one of this plurality of VGAM775 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM775 RNA, herein designated VGAM RNA, and which when bound by VGAM775 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM775 host target proteins.

[10813] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM775 gene, herein designated VGAM GENE, on one or more VGAM775 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10814] It is yet further appreciated that a function of VGAM775 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM775 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM775 correlate with, and may be deduced from, the

identity of the host target genes which VGAM775 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10815] Nucleotide sequences of the VGAM775 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM775 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM775 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM775 are further described hereinbelow with reference to Table 1.

[10816] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM775 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10817] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 776 (VGAM776) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10818] VGAM776 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM776 was detected is described hereinabove with reference to Figs. 2–8.

[10819] VGAM776 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM776 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10820] VGAM776 gene, herein designated VGAM GENE, encodes a VGAM776 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM776 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM776 precursor RNA is designated SEQ ID:21128, and is provided hereinbelow with reference to the sequence listing part.

[10821] VGAM776 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM776 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10822] An enzyme complex designated DICER COMPLEX, dices the VGAM776 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM776 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM776 RNA is designated SEQ ID:21129, and is provided hereinbelow with reference to the sequence listing part.

[10823] VGAM776 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM776 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM776 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5



untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10824] VGAM776 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM776 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM776 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM776 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM776 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10825] The complementary binding of VGAM776 RNA, herein designated VGAM RNA, to host target binding sites on VGAM776 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM776 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM776 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10826] It is appreciated that VGAM776 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM776 host target genes. The mRNA of each one of this plurality of VGAM776 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM776 RNA, herein designated VGAM RNA, and which when bound by VGAM776 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM776 host target proteins.

[10827] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM776 gene, herein designated VGAM GENE, on one or more VGAM776 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10828] It is yet further appreciated that a function of VGAM776 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM776 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM776 correlate with, and may be deduced from, the identity of the host target genes which VGAM776 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10829] Nucleotide sequences of the VGAM776 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM776 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM776 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM776 are further described hereinbelow with reference to Table 1.

[10830] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM776 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10831] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 777 (VGAM777) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10832] VGAM777 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM777 was detected is described hereinabove with reference to Figs. 2–8.

[10833] VGAM777 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet mild yellowing virus. VGAM777 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10834] VGAM777 gene, herein designated VGAM GENE, encodes a VGAM777 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM777 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM777 precursor RNA is designated SEQ ID:21134, and is provided hereinbelow with reference to the sequence listing part.

[10835] VGAM777 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM777 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10836] An enzyme complex designated DICER COMPLEX, dices the VGAM777 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM777 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM777 RNA is designated SEQ ID:21135, and is provided hereinbelow with reference to the sequence listing part.

[10837] VGAM777 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM777 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM777 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10838] VGAM777 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM777 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM777 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM777 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM777 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[10839] The complementary binding of VGAM777 RNA, herein designated VGAM RNA, to host target binding sites on VGAM777 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM777 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM777 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10840] It is appreciated that VGAM777 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM777 host target genes. The mRNA of each one of this plurality of VGAM777 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM777 RNA, herein designated VGAM RNA, and which when bound by VGAM777 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM777 host target proteins.

[10841] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM777 gene, herein designated VGAM GENE, on one or more VGAM777 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10842] It is yet further appreciated that a function of VGAM777 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM777 include diagnosis, prevention and treatment of viral infection by Beet mild yellowing virus. Specific functions, and accordingly utilities, of VGAM777 correlate with, and may be deduced from, the identity of the host target genes which VGAM777 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[10843] Nucleotide sequences of the VGAM777 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM777 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM777 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM777 are further described hereinbelow with reference to Table 1.

[10844] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM777 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10845] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 778 (VGAM778) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10846] VGAM778 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM778 was detected is described hereinabove with reference to Figs. 2–8.

[10847] VGAM778 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet mild yellowing virus. VGAM778 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10848] VGAM778 gene, herein designated VGAM GENE, encodes a VGAM778 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM778 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM778 precursor RNA is designated SEQ ID:21151, and is provided hereinbelow with reference to the sequence listing part.

[10849] VGAM778 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM778 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10850] An enzyme complex designated DICER COMPLEX, dices the VGAM778 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM778 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM778 RNA is designated SEQ ID:21152, and is provided hereinbelow with reference to the sequence listing part.

[10851] VGAM778 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM778 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM778 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[10852] VGAM778 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM778 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM778 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM778 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM778 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10853] The complementary binding of VGAM778 RNA, herein designated VGAM RNA, to host target binding sites on VGAM778 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM778 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM778 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10854] It is appreciated that VGAM778 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM778 host target genes. The mRNA of each one of this plurality of VGAM778 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM778 RNA, herein designated VGAM RNA, and which when bound by VGAM778 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM778 host target proteins.

[10855] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM778 gene, herein designated VGAM GENE, on one or

more VGAM778 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10856] It is yet further appreciated that a function of VGAM778 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM778 include diagnosis, prevention and treatment of viral infection by Beet mild yellowing virus. Specific functions, and accordingly utilities, of VGAM778 correlate with, and may be deduced from, the identity of the host target genes which VGAM778 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10857] Nucleotide sequences of the VGAM778 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM778 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM778 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM778 are further described hereinbelow with reference to Table 1.

[10858] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM778 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10859] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 779 (VGAM779) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10860] VGAM779 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM779 was detected is described



hereinabove with reference to Figs. 2–8.

[10861] VGAM779 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet mild yellowing virus. VGAM779 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10862] VGAM779 gene, herein designated VGAM GENE, encodes a VGAM779 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM779 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM779 precursor RNA is designated SEQ ID:21156, and is provided hereinbelow with reference to the sequence listing part.

[10863] VGAM779 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM779 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10864] An enzyme complex designated DICER COMPLEX, dices the VGAM779 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM779 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM779 RNA is designated SEQ ID:21157, and is provided hereinbelow with reference to the sequence listing part.

[10865] VGAM779 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM779 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM779 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10866] VGAM779 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM779 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM779 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM779 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM779 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10867] The complementary binding of VGAM779 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM779 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM779 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM779 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10868] It is appreciated that VGAM779 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM779 host target genes. The mRNA of each one of this plurality of VGAM779 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM779 RNA, herein designated VGAM RNA, and which when bound by VGAM779 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM779 host target proteins.

[10869] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM779 gene, herein designated VGAM GENE, on one or more VGAM779 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10870] It is yet further appreciated that a function of VGAM779 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM779 include diagnosis, prevention and treatment of viral infection by Beet mild yellowing virus. Specific functions, and accordingly utilities, of VGAM779 correlate with, and may be deduced from, the identity of the host target genes which VGAM779 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10871] Nucleotide sequences of the VGAM779 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM779 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM779 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM779 are further described hereinbelow with reference to Table 1.

[10872] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM779 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10873] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 780 (VGAM780) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10874] VGAM780 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM780 was detected is described hereinabove with reference to Figs. 2-8.

[10875] VGAM780 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet mild yellowing virus. VGAM780 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10876] VGAM780 gene, herein designated VGAM GENE, encodes a VGAM780 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM780 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM780 precursor RNA is designated SEQ ID:21166, and is provided hereinbelow with reference to the sequence listing part.

[10877] VGAM780 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM780 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[10878] An enzyme complex designated DICER COMPLEX, dices the VGAM780 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM780 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM780 RNA is designated SEQ ID:21167, and is provided hereinbelow with reference to the sequence listing part.

[10879] VGAM780 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM780 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM780 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10880] VGAM780 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM780 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM780 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM780 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM780 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10881] The complementary binding of VGAM780 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM780 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM780 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM780 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10882] It is appreciated that VGAM780 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM780 host target genes. The mRNA of each one of this plurality of VGAM780 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM780 RNA, herein designated VGAM RNA, and which when bound by VGAM780 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM780 host target proteins.

[10883] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM780 gene, herein designated VGAM GENE, on one or more VGAM780 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10884] It is yet further appreciated that a function of VGAM780 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM780 include diagnosis, prevention and treatment of viral infection by Beet mild yellowing virus. Specific functions, and accordingly utilities, of VGAM780 correlate with, and may be deduced from, the identity of the host target genes which VGAM780 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10885] Nucleotide sequences of the VGAM780 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM780 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM780 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM780 are further described hereinbelow with reference to Table 1.

[10886] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM780 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10887] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 781 (VGAM781) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10888] VGAM781 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM781 was detected is described hereinabove with reference to Figs. 2-8.

[10889] VGAM781 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Beet mild yellowing virus. VGAM781 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10890] VGAM781 gene, herein designated VGAM GENE, encodes a VGAM781 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM781 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM781 precursor RNA is designated SEQ ID:21232, and is provided hereinbelow with reference to the sequence listing part.

[10891] VGAM781 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM781 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10892] An enzyme complex designated DICER COMPLEX, dices the VGAM781 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM781 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM781 RNA is designated SEQ ID:21233, and is provided hereinbelow with reference to the sequence listing part.

[10893] VGAM781 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM781 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM781 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10894] VGAM781 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM781 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM781 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM781 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM781 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10895] The complementary binding of VGAM781 RNA, herein designated VGAM RNA, to host target binding sites on VGAM781 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM781 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM781 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10896] It is appreciated that VGAM781 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM781 host target genes. The mRNA of each one of this plurality of VGAM781 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM781 RNA, herein designated VGAM RNA, and which when bound by VGAM781 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM781 host target proteins.

[10897] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM781 gene, herein designated VGAM GENE, on one or more VGAM781 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10898] It is yet further appreciated that a function of VGAM781 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM781 include diagnosis, prevention and treatment of viral infection by Beet mild yellowing virus. Specific functions, and accordingly utilities, of VGAM781 correlate with, and may be deduced from, the identity of the host target genes which VGAM781 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10899] Nucleotide sequences of the VGAM781 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM781 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM781 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM781 are further described hereinbelow with reference to Table 1.

[10900] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM781 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10901] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 782 (VGAM782) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10902] VGAM782 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM782 was detected is described hereinabove with reference to Figs. 2-8.

[10903] VGAM782 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet mild yellowing

virus. VGAM782 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10904] VGAM782 gene, herein designated VGAM GENE, encodes a VGAM782 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM782 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM782 precursor RNA is designated SEQ ID:21249, and is provided hereinbelow with reference to the sequence listing part.

[10905] VGAM782 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM782 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10906] An enzyme complex designated DICER COMPLEX, dices

the VGAM782 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM782 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM782 RNA is designated SEQ ID:21250, and is provided hereinbelow with reference to the sequence listing part.

[10907] VGAM782 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM782 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM782 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10908] VGAM782 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM782 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM782 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM782 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM782 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10909] The complementary binding of VGAM782 RNA, herein designated VGAM RNA, to host target binding sites on VGAM782 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM782 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM782 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10910] It is appreciated that VGAM782 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM782 host target genes. The mRNA of each one of this plurality of VGAM782 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM782 RNA, herein designated VGAM RNA, and which when bound by VGAM782 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM782 host target proteins.

[10911] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM782 gene, herein designated VGAM GENE, on one or more VGAM782 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10912] It is yet further appreciated that a function of VGAM782 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM782 include diagnosis, prevention and treatment of viral infection by Beet mild yellowing virus. Specific functions, and accordingly utilities, of VGAM782 correlate with, and may be deduced from, the identity of the host target genes which VGAM782 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10913] Nucleotide sequences of the VGAM782 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM782 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM782 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM782 are further described hereinbelow with reference to Table 1.

[10914] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM782 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10915] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 783 (VGAM783) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10916] VGAM783 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM783 was detected is described hereinabove with reference to Figs. 2-8.

[10917] VGAM783 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM783 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[10918] VGAM783 gene, herein designated VGAM GENE, encodes a VGAM783 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM783 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM783 precursor RNA is designated SEQ ID:21291, and is provided hereinbelow with reference to the sequence listing part.

[10919] VGAM783 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM783 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10920] An enzyme complex designated DICER COMPLEX, dices the VGAM783 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM783 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM783 RNA is designated SEQ ID:21292, and is provided hereinbelow with reference to the sequence listing part.

[10921] VGAM783 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM783 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM783 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10922] VGAM783 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM783 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM783 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM783 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM783 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10923] The complementary binding of VGAM783 RNA, herein designated VGAM RNA, to host target binding sites on VGAM783 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM783 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM783 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10924] It is appreciated that VGAM783 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM783 host target genes. The mRNA of each one of this plurality of VGAM783 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM783 RNA, herein designated VGAM RNA, and which when bound by VGAM783 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM783 host target proteins.

[10925] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM783 gene, herein designated VGAM GENE, on one or more VGAM783 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10926] It is yet further appreciated that a function of VGAM783 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM783 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM783 correlate with, and may be deduced from, the identity of the host target genes which VGAM783 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10927] Nucleotide sequences of the VGAM783 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM783 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM783 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM783 are further described hereinbelow with reference to Table 1.

[10928] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM783 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10929] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 784 (VGAM784) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10930] VGAM784 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM784 was detected is described hereinabove with reference to Figs. 2-8.

[10931] VGAM784 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM784 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[10932] VGAM784 gene, herein designated VGAM GENE, encodes a VGAM784 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM784 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM784 precursor RNA is designated SEQ ID:21308, and is provided hereinbelow with reference to the sequence listing part.

[10933] VGAM784 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM784 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10934] An enzyme complex designated DICER COMPLEX, dices the VGAM784 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM784 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM784 RNA is designated SEQ ID:21309, and is provided hereinbelow with reference to the sequence listing part.

[10935] VGAM784 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM784 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM784 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10936] VGAM784 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM784 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM784 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM784 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM784 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10937] The complementary binding of VGAM784 RNA, herein designated VGAM RNA, to host target binding sites on VGAM784 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM784 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM784 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10938] It is appreciated that VGAM784 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM784 host target genes. The mRNA of each one of this plurality of VGAM784 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM784 RNA, herein designated VGAM RNA, and which when bound by VGAM784 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM784 host target proteins.

[10939] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM784 gene, herein designated VGAM GENE, on one or more VGAM784 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10940] It is yet further appreciated that a function of VGAM784 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM784 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM784 correlate with, and may be deduced from, the identity of the host target genes which VGAM784 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10941] Nucleotide sequences of the VGAM784 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM784 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM784 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM784 are further de-

scribed hereinbelow with reference to Table 1.

[10942] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM784 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10943] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 785 (VGAM785) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10944] VGAM785 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM785 was detected is described hereinabove with reference to Figs. 2-8.

[10945] VGAM785 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM785 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10946] VGAM785 gene, herein designated VGAM GENE, encodes a VGAM785 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM785 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM785 precursor RNA is designated SEQ ID:21331, and is provided hereinbelow with reference to the sequence listing part.

[10947] VGAM785 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM785 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10948] An enzyme complex designated DICER COMPLEX, dices the VGAM785 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM785 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM785 RNA is designated SEQ ID:21332, and is provided hereinbelow with reference to the sequence listing part.

[10949] VGAM785 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM785 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM785 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10950] VGAM785 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM785 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM785 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM785 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM785 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10951] The complementary binding of VGAM785 RNA, herein designated VGAM RNA, to host target binding sites on VGAM785 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM785 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM785 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10952] It is appreciated that VGAM785 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM785 host target genes. The mRNA of each one of this plurality of VGAM785 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM785 RNA, herein designated VGAM RNA, and which when bound by VGAM785 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM785 host target proteins.

[10953] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM785 gene, herein designated VGAM GENE, on one or more VGAM785 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10954] It is yet further appreciated that a function of VGAM785 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM785 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM785 correlate with, and may be deduced from, the identity of the host target genes which VGAM785 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10955] Nucleotide sequences of the VGAM785 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM785 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM785 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM785 are further described hereinbelow with reference to Table 1.

[10956] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM785 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10957] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 786 (VGAM786) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10958] VGAM786 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM786 was detected is described hereinabove with reference to Figs. 2-8.

[10959] VGAM786 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM786 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10960] VGAM786 gene, herein designated VGAM GENE, encodes a

VGAM786 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM786 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM786 precursor RNA is designated SEQ ID:21351, and is provided hereinbelow with reference to the sequence listing part.

[10961] VGAM786 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM786 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10962] An enzyme complex designated DICER COMPLEX, dices the VGAM786 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM786 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM786 RNA is designated SEQ ID:21352, and is provided hereinbelow with reference to the sequence listing part.

[10963] VGAM786 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM786 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM786 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10964] VGAM786 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM786 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM786 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM786 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM786 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10965] The complementary binding of VGAM786 RNA, herein designated VGAM RNA, to host target binding sites on VGAM786 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM786 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM786 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[10966] It is appreciated that VGAM786 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM786 host target genes. The mRNA of each one of this plurality of VGAM786 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM786 RNA, herein designated VGAM RNA, and which when bound by VGAM786 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM786 host target proteins.

[10967] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM786 gene, herein designated VGAM GENE, on one or more VGAM786 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10968] It is yet further appreciated that a function of VGAM786 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM786 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM786 correlate with, and may be deduced from, the identity of the host target genes which VGAM786 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10969] Nucleotide sequences of the VGAM786 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM786 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM786 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM786 are further described hereinbelow with reference to Table 1.

[10970] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM786 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10971] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 787 (VGAM787) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10972] VGAM787 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM787 was detected is described hereinabove with reference to Figs. 2-8.

[10973] VGAM787 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM787 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10974] VGAM787 gene, herein designated VGAM GENE, encodes a VGAM787 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM787 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM787 precursor RNA is designated SEQ ID:21357, and is provided hereinbelow with reference to the sequence listing part.

[10975] VGAM787 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM787 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10976] An enzyme complex designated DICER COMPLEX, dices the VGAM787 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM787 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM787 RNA is designated SEQ ID:21358, and is provided hereinbelow with reference to the sequence listing part.

[10977] VGAM787 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM787 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM787 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10978] VGAM787 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM787 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM787 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM787 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM787 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10979] The complementary binding of VGAM787 RNA, herein designated VGAM RNA, to host target binding sites on VGAM787 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM787 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM787 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10980] It is appreciated that VGAM787 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM787 host target genes. The mRNA of each one of this plurality of VGAM787 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM787 RNA, herein designated VGAM RNA, and which when bound by VGAM787 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM787 host target proteins.

[10981] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM787 gene, herein designated VGAM GENE, on one or more VGAM787 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10982] It is yet further appreciated that a function of VGAM787 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM787 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM787 correlate with, and may be deduced from, the identity of the host target genes which VGAM787 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10983] Nucleotide sequences of the VGAM787 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM787 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM787 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM787 are further described hereinbelow with reference to Table 1.

[10984] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM787 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10985] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 788 (VGAM788) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10986] VGAM788 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM788 was detected is described hereinabove with reference to Figs. 2–8.

[10987] VGAM788 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM788 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10988] VGAM788 gene, herein designated VGAM GENE, encodes a VGAM788 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM788 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM788 precursor RNA is designated SEQ ID:21360, and is provided hereinbelow with reference to the sequence listing part.

[10989] VGAM788 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM788 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10990] An enzyme complex designated DICER COMPLEX, dices the VGAM788 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM788 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM788 RNA is designated SEQ ID:21361, and is provided hereinbelow with reference to the sequence listing part.

[10991] VGAM788 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM788 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM788 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[10992] VGAM788 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM788 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM788 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM788 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM788 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[10993] The complementary binding of VGAM788 RNA, herein designated VGAM RNA, to host target binding sites on VGAM788 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM788 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM788 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10994] It is appreciated that VGAM788 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM788 host target genes. The mRNA of each one of this plurality of VGAM788 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM788 RNA, herein designated VGAM RNA, and which when bound by VGAM788 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM788 host target proteins.

[10995] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM788 gene, herein designated VGAM GENE, on one or more VGAM788 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[10996] It is yet further appreciated that a function of VGAM788 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM788 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM788 correlate with, and may be deduced from, the identity of the host target genes which VGAM788 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10997] Nucleotide sequences of the VGAM788 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM788 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM788 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM788 are further described hereinbelow with reference to Table 1.

[10998] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM788 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10999] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 789 (VGAM789) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11000] VGAM789 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM789 was detected is described hereinabove with reference to Figs. 2–8.

[11001] VGAM789 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus.

VGAM789 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11002] VGAM789 gene, herein designated VGAM GENE, encodes a VGAM789 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM789 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM789 precursor RNA is designated SEQ ID:21385, and is provided hereinbelow with reference to the sequence listing part.

[11003] VGAM789 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM789 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11004] An enzyme complex designated DICER COMPLEX, dices the VGAM789 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM789 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 55%) nucleotide sequence of VGAM789 RNA is designated SEQ ID:21386, and is provided hereinbelow with reference to the sequence listing part.

[11005] VGAM789 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM789 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM789 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11006] VGAM789 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM789 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM789 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM789 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM789 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11007] The complementary binding of VGAM789 RNA, herein designated VGAM RNA, to host target binding sites on VGAM789 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM789 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM789 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11008] It is appreciated that VGAM789 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM789 host target genes. The mRNA of each one of this plurality of VGAM789 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM789 RNA, herein designated VGAM RNA, and which when bound by VGAM789 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM789 host target proteins.

[11009] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM789 gene, herein designated VGAM GENE, on one or more VGAM789 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[11010] It is yet further appreciated that a function of VGAM789 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM789 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM789 correlate with, and may be deduced from, the identity of the host target genes which VGAM789 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[11011] Nucleotide sequences of the VGAM789 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM789 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM789 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM789 are further described hereinbelow with reference to Table 1.

[11012] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM789 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11013] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 790 (VGAM790) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11014] VGAM790 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM790 was detected is described hereinabove with reference to Figs. 2–8.

[11015] VGAM790 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM790 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11016] VGAM790 gene, herein designated VGAM GENE, encodes a VGAM790 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM790 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM790 precursor RNA is designated SEQ ID:21389, and is provided hereinbelow with reference to the sequence listing part.

[11017] VGAM790 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM790 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11018] An enzyme complex designated DICER COMPLEX, dices the VGAM790 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM790 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM790 RNA is designated SEQ ID:21390, and is provided hereinbelow with reference to the sequence listing part.

[11019] VGAM790 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM790 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM790 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11020] VGAM790 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM790 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM790 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM790 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM790 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11021] The complementary binding of VGAM790 RNA, herein designated VGAM RNA, to host target binding sites on VGAM790 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM790 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM790 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11022] It is appreciated that VGAM790 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM790 host target genes. The mRNA of

each one of this plurality of VGAM790 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM790 RNA, herein designated VGAM RNA, and which when bound by VGAM790 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM790 host target proteins.

[11023] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM790 gene, herein designated VGAM GENE, on one or more VGAM790 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[11024] It is yet further appreciated that a function of VGAM790 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM790 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM790 correlate with, and may be deduced from, the identity of the host target genes which VGAM790 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11025] Nucleotide sequences of the VGAM790 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM790 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM790 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM790 are further described hereinbelow with reference to Table 1.

[11026] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM790 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[11027] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 791 (VGAM791) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11028] VGAM791 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM791 was detected is described hereinabove with reference to Figs. 2–8.

[11029] VGAM791 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM791 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11030] VGAM791 gene, herein designated VGAM GENE, encodes a VGAM791 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM791 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar



to the nucleotide sequence of VGAM791 precursor RNA is designated SEQ ID:21395, and is provided hereinbelow with reference to the sequence listing part.

[11031] VGAM791 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM791 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11032] An enzyme complex designated DICER COMPLEX, dices the VGAM791 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM791 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM791 RNA is designated SEQ ID:21396, and

is provided hereinbelow with reference to the sequence listing part.

[11033] VGAM791 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM791 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM791 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11034] VGAM791 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM791 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM791 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM791 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM791 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11035] The complementary binding of VGAM791 RNA, herein designated VGAM RNA, to host target binding sites on VGAM791 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM791 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM791 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11036] It is appreciated that VGAM791 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM791 host target genes. The mRNA of each one of this plurality of VGAM791 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM791 RNA, herein designated VGAM RNA, and which when bound by VGAM791 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM791 host target proteins.

[11037] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM791 gene, herein designated VGAM GENE, on one or more VGAM791 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11038] It is yet further appreciated that a function of VGAM791 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM791 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM791 correlate with, and may be deduced from, the identity of the host target genes which VGAM791 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11039] Nucleotide sequences of the VGAM791 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM791 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM791 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM791 are further described hereinbelow with reference to Table 1.

[11040] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM791 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11041] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 792 (VGAM792) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11042] VGAM792 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM792 was detected is described hereinabove with reference to Figs. 2–8.

[11043] VGAM792 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus. VGAM792 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11044] VGAM792 gene, herein designated VGAM GENE, encodes a VGAM792 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM792 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM792 precursor RNA is

designated SEQ ID:21400, and is provided hereinbelow with reference to the sequence listing part.

[11045] VGAM792 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM792 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11046] An enzyme complex designated DICER COMPLEX, dices the VGAM792 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM792 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM792 RNA is designated SEQ ID:21401, and is provided hereinbelow with reference to the sequence

listing part.

[11047] VGAM792 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM792 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM792 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11048] VGAM792 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM792 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM792 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM792 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM792 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11049] The complementary binding of VGAM792 RNA, herein designated VGAM RNA, to host target binding sites on VGAM792 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM792 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM792 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11050] It is appreciated that VGAM792 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM792 host target genes. The mRNA of each one of this plurality of VGAM792 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM792 RNA, herein designated VGAM RNA, and which when bound by VGAM792 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM792 host target proteins.

[11051] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM792 gene, herein designated VGAM GENE, on one or more VGAM792 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11052] It is yet further appreciated that a function of VGAM792 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM792 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM792 correlate with, and may be deduced from, the identity of the host target genes which VGAM792 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11053] Nucleotide sequences of the VGAM792 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM792 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM792 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM792 are further described hereinbelow with reference to Table 1.

[11054] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM792 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11055] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 793 (VGAM793) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11056] VGAM793 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM793 was detected is described hereinabove with reference to Figs. 2–8.

[11057] VGAM793 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet chlorosis virus. VGAM793 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11058] VGAM793 gene, herein designated VGAM GENE, encodes a VGAM793 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM793 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM793 precursor RNA is designated SEQ ID:21423, and is provided hereinbelow

with reference to the sequence listing part.

[11059] VGAM793 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM793 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11060] An enzyme complex designated DICER COMPLEX, dices the VGAM793 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM793 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM793 RNA is designated SEQ ID:21424, and is provided hereinbelow with reference to the sequence listing part.

[11061] VGAM793 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM793 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM793 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11062] VGAM793 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM793 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM793 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM793 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM793 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11063] The complementary binding of VGAM793 RNA, herein designated VGAM RNA, to host target binding sites on VGAM793 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM793 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM793 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11064] It is appreciated that VGAM793 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM793 host target genes. The mRNA of each one of this plurality of VGAM793 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM793 RNA, herein designated VGAM RNA, and which when bound by VGAM793 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM793 host target proteins.

[11065] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM793 gene, herein designated VGAM GENE, on one or more VGAM793 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11066] It is yet further appreciated that a function of VGAM793 is inhibition of expression of host target genes, as part of a



novel viral mechanism of attacking a host. Accordingly, utilities of VGAM793 include diagnosis, prevention and treatment of viral infection by Beet chlorosis virus. Specific functions, and accordingly utilities, of VGAM793 correlate with, and may be deduced from, the identity of the host target genes which VGAM793 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11067] Nucleotide sequences of the VGAM793 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM793 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM793 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM793 are further described hereinbelow with reference to Table 1.

[11068] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM793 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11069] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 794 (VGAM794) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11070] VGAM794 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM794 was detected is described hereinabove with reference to Figs. 2–8.

[11071] VGAM794 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM794 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11072] VGAM794 gene, herein designated VGAM GENE, encodes a VGAM794 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM794 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM794 precursor RNA is designated SEQ ID:21440, and is provided hereinbelow with reference to the sequence listing part.

[11073] VGAM794 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM794 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11074] An enzyme complex designated DICER COMPLEX, dices the VGAM794 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM794 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM794 RNA is designated SEQ ID:21441, and is provided hereinbelow with reference to the sequence listing part.

[11075] VGAM794 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM794 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM794 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11076] VGAM794 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM794 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM794 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM794 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM794 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11077] The complementary binding of VGAM794 RNA, herein designated VGAM RNA, to host target binding sites on VGAM794 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM794 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM794 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11078] It is appreciated that VGAM794 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM794 host target genes. The mRNA of each one of this plurality of VGAM794 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM794 RNA, herein designated VGAM

RNA, and which when bound by VGAM794 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM794 host target proteins.

[11079] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM794 gene, herein designated VGAM GENE, on one or more VGAM794 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11080] It is yet further appreciated that a function of VGAM794 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM794 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM794 correlate with, and may be deduced from, the identity of the host target genes which VGAM794 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11081] Nucleotide sequences of the VGAM794 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM794 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM794 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM794 are further described hereinbelow with reference to Table 1.

[11082] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM794 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11083] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 795 (VGAM795) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11084] VGAM795 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM795 was detected is described hereinabove with reference to Figs. 2–8.

[11085] VGAM795 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM795 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11086] VGAM795 gene, herein designated VGAM GENE, encodes a VGAM795 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM795 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM795 precursor RNA is designated SEQ ID:21444, and is provided hereinbelow with reference to the sequence listing part.

[11087] VGAM795 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM795 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11088] An enzyme complex designated DICER COMPLEX, dices the VGAM795 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM795 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM795 RNA is designated SEQ ID:21445, and is provided hereinbelow with reference to the sequence listing part.

[11089] VGAM795 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM795 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM795 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11090] VGAM795 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM795 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM795 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM795 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM795 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11091] The complementary binding of VGAM795 RNA, herein designated VGAM RNA, to host target binding sites on VGAM795 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM795 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM795 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11092] It is appreciated that VGAM795 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM795 host target genes. The mRNA of each one of this plurality of VGAM795 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM795 RNA, herein designated VGAM RNA, and which when bound by VGAM795 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM795 host target proteins.

[11093] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM795 gene, herein designated VGAM GENE, on one or more VGAM795 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11094] It is yet further appreciated that a function of VGAM795 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM795 include diagnosis, prevention and

treatment of viral infection by Mollusum contagiosum virus. Specific functions, and accordingly utilities, of VGAM795 correlate with, and may be deduced from, the identity of the host target genes which VGAM795 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11095] Nucleotide sequences of the VGAM795 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM795 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM795 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM795 are further described hereinbelow with reference to Table 1.

[11096] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM795 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11097] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 796 (VGAM796) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11098] VGAM796 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM796 was detected is described hereinabove with reference to Figs. 2–8.

[11099] VGAM796 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM796 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11100] VGAM796 gene, herein designated VGAM GENE, encodes a VGAM796 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM796 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM796 precursor RNA is designated SEQ ID:21448, and is provided hereinbelow with reference to the sequence listing part.

[11101] VGAM796 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM796 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11102] An enzyme complex designated DICER COMPLEX, dices the VGAM796 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM796 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM796 RNA is designated SEQ ID:21449, and is provided hereinbelow with reference to the sequence listing part.

[11103] VGAM796 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM796 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM796 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11104] VGAM796 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM796 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM796 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM796 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM796 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11105] The complementary binding of VGAM796 RNA, herein designated VGAM RNA, to host target binding sites on VGAM796 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM796 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM796 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11106] It is appreciated that VGAM796 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM796 host target genes. The mRNA of each one of this plurality of VGAM796 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM796 RNA, herein designated VGAM RNA, and which when bound by VGAM796 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM796 host target proteins.

[11107] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM796 gene, herein designated VGAM GENE, on one or more VGAM796 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11108] It is yet further appreciated that a function of VGAM796 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM796 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Spe-

cific functions, and accordingly utilities, of VGAM796 correlate with, and may be deduced from, the identity of the host target genes which VGAM796 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [11109] Nucleotide sequences of the VGAM796 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM796 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM796 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM796 are further described hereinbelow with reference to Table 1.
- [11110] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM796 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [11111] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 797 (VGAM797) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[11112] VGAM797 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM797 was detected is described hereinabove with reference to Figs. 2–8.

[11113] VGAM797 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus. VGAM797 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11114] VGAM797 gene, herein designated VGAM GENE, encodes a VGAM797 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM797 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM797 precursor RNA is designated SEQ ID:21491, and is provided hereinbelow with reference to the sequence listing part.

[11115] VGAM797 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM797 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11116] An enzyme complex designated DICER COMPLEX, dices the VGAM797 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM797 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM797 RNA is designated SEQ ID:21492, and is provided hereinbelow with reference to the sequence listing part.

[11117] VGAM797 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM797 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM797 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11118] VGAM797 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM797 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM797 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM797 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM797 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11119] The complementary binding of VGAM797 RNA, herein designated VGAM RNA, to host target binding sites on VGAM797 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM797 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM797 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11120] It is appreciated that VGAM797 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM797 host target genes. The mRNA of each one of this plurality of VGAM797 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM797 RNA, herein designated VGAM RNA, and which when bound by VGAM797 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM797 host target proteins.

[11121] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM797 gene, herein designated VGAM GENE, on one or more VGAM797 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11122] It is yet further appreciated that a function of VGAM797 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM797 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM797 correlate



with, and may be deduced from, the identity of the host target genes which VGAM797 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11123] Nucleotide sequences of the VGAM797 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM797 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM797 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM797 are further described hereinbelow with reference to Table 1.

[11124] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM797 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11125] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 798 (VGAM798) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[11126] VGAM798 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM798 was detected is described hereinabove with reference to Figs. 2–8.

[11127] VGAM798 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus. VGAM798 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11128] VGAM798 gene, herein designated VGAM GENE, encodes a VGAM798 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM798 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM798 precursor RNA is designated SEQ ID:21503, and is provided hereinbelow with reference to the sequence listing part.

[11129] VGAM798 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM798 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11130] An enzyme complex designated DICER COMPLEX, dices the VGAM798 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM798 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM798 RNA is designated SEQ ID:21504, and is provided hereinbelow with reference to the sequence listing part.

[11131] VGAM798 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM798 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM798 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11132] VGAM798 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM798 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM798 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM798 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM798 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11133] The complementary binding of VGAM798 RNA, herein designated VGAM RNA, to host target binding sites on VGAM798 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM798 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM798 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11134] It is appreciated that VGAM798 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM798 host target genes. The mRNA of each one of this plurality of VGAM798 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM798 RNA, herein designated VGAM RNA, and which when bound by VGAM798 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM798 host target proteins.

[11135] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM798 gene, herein designated VGAM GENE, on one or more VGAM798 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11136] It is yet further appreciated that a function of VGAM798 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM798 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM798 correlate with, and may be deduced from, the identity of the host

target genes which VGAM798 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11137] Nucleotide sequences of the VGAM798 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM798 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM798 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM798 are further described hereinbelow with reference to Table 1.

[11138] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM798 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11139] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 799 (VGAM799) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11140] VGAM799 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM799 was detected is described hereinabove with reference to Figs. 2–8.

[11141] VGAM799 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM799 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11142] VGAM799 gene, herein designated VGAM GENE, encodes a VGAM799 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM799 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM799 precursor RNA is designated SEQ ID:21635, and is provided hereinbelow with reference to the sequence listing part.

[11143] VGAM799 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM799 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11144] An enzyme complex designated DICER COMPLEX, dices the VGAM799 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM799 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM799 RNA is designated SEQ ID:21636, and is provided hereinbelow with reference to the sequence listing part.

[11145] VGAM799 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM799 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM799 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11146] VGAM799 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM799 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM799 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM799 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM799 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11147] The complementary binding of VGAM799 RNA, herein designated VGAM RNA, to host target binding sites on VGAM799 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM799 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM799 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11148] It is appreciated that VGAM799 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM799 host target genes. The mRNA of each one of this plurality of VGAM799 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM799 RNA, herein designated VGAM RNA, and which when bound by VGAM799 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM799 host target proteins.

[11149] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM799 gene, herein designated VGAM GENE, on one or more VGAM799 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11150] It is yet further appreciated that a function of VGAM799 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM799 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM799 correlate with, and may be deduced from, the identity of the host target genes which VGAM799 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[11151] Nucleotide sequences of the VGAM799 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM799 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM799 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM799 are further described hereinbelow with reference to Table 1.

[11152] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM799 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11153] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 800 (VGAM800) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11154] VGAM800 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM800 was detected is described hereinabove with reference to Figs. 2–8.

[11155] VGAM800 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus.

VGAM800 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11156] VGAM800 gene, herein designated VGAM GENE, encodes a VGAM800 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM800 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM800 precursor RNA is designated SEQ ID:21658, and is provided hereinbelow with reference to the sequence listing part.

[11157] VGAM800 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM800 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11158] An enzyme complex designated DICER COMPLEX, dices the VGAM800 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM800 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM800 RNA is designated SEQ ID:21659, and is provided hereinbelow with reference to the sequence listing part.

[11159] VGAM800 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM800 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM800 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11160] VGAM800 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM800 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM800 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM800 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM800 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3'UTR and 5'UTR regions.

[11161] The complementary binding of VGAM800 RNA, herein designated VGAM RNA, to host target binding sites on VGAM800 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM800 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM800 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11162] It is appreciated that VGAM800 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM800 host target genes. The mRNA of each one of this plurality of VGAM800 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM800 RNA, herein designated VGAM RNA, and which when bound by VGAM800 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM800 host target proteins.

[11163] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM800 gene, herein designated VGAM GENE, on one or more VGAM800 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11164] It is yet further appreciated that a function of VGAM800 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM800 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM800 correlate with, and may be deduced from, the identity of the host target genes which VGAM800 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[11165] Nucleotide sequences of the VGAM800 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM800 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM800 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM800 are further described hereinbelow with reference to Table 1.

[11166] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM800 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11167] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 801 (VGAM801) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11168] VGAM801 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM801 was detected is described hereinabove with reference to Figs. 2–8.

[11169] VGAM801 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus.

VGAM801 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11170] VGAM801 gene, herein designated VGAM GENE, encodes a VGAM801 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM801 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM801 precursor RNA is designated SEQ ID:21682, and is provided hereinbelow with reference to the sequence listing part.

[11171] VGAM801 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM801 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11172] An enzyme complex designated DICER COMPLEX, dices the VGAM801 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM801 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM801 RNA is designated SEQ ID:21683, and is provided hereinbelow with reference to the sequence listing part.

[11173] VGAM801 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM801 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM801 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[11174] VGAM801 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM801 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM801 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM801 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM801 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11175] The complementary binding of VGAM801 RNA, herein designated VGAM RNA, to host target binding sites on VGAM801 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM801 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM801 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11176] It is appreciated that VGAM801 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM801 host target genes. The mRNA of each one of this plurality of VGAM801 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM801 RNA, herein designated VGAM RNA, and which when bound by VGAM801 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM801 host target proteins.

[11177] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM801 gene, herein designated VGAM GENE, on one or

more VGAM801 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11178] It is yet further appreciated that a function of VGAM801 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM801 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM801 correlate with, and may be deduced from, the identity of the host target genes which VGAM801 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[11179] Nucleotide sequences of the VGAM801 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM801 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM801 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM801 are further described hereinbelow with reference to Table 1.

[11180] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM801 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11181] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 802 (VGAM802) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11182] VGAM802 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM802 was detected is described

hereinabove with reference to Figs. 2–8.

[11183] VGAM802 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus.

VGAM802 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11184] VGAM802 gene, herein designated VGAM GENE, encodes a VGAM802 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM802 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM802 precursor RNA is designated SEQ ID:21701, and is provided hereinbelow with reference to the sequence listing part.

[11185] VGAM802 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM802 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11186] An enzyme complex designated DICER COMPLEX, dices the VGAM802 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM802 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM802 RNA is designated SEQ ID:21702, and is provided hereinbelow with reference to the sequence listing part.

[11187] VGAM802 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM802 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM802 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11188] VGAM802 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM802 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM802 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM802 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM802 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11189] The complementary binding of VGAM802 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM802 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM802 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM802 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11190] It is appreciated that VGAM802 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM802 host target genes. The mRNA of each one of this plurality of VGAM802 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM802 RNA, herein designated VGAM RNA, and which when bound by VGAM802 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM802 host target proteins.

[11191] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM802 gene, herein designated VGAM GENE, on one or more VGAM802 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11192] It is yet further appreciated that a function of VGAM802 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM802 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM802 correlate with, and may be deduced from, the identity of the host target genes which VGAM802 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11193] Nucleotide sequences of the VGAM802 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM802 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM802 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM802 are further described hereinbelow with reference to Table 1.

[11194] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM802 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11195] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 803 (VGAM803) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11196] VGAM803 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM803 was detected is described hereinabove with reference to Figs. 2-8.

[11197] VGAM803 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus.

VGAM803 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11198] VGAM803 gene, herein designated VGAM GENE, encodes a VGAM803 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM803 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM803 precursor RNA is designated SEQ ID:21708, and is provided hereinbelow with reference to the sequence listing part.

[11199] VGAM803 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM803 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[11200] An enzyme complex designated DICER COMPLEX, dices the VGAM803 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM803 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM803 RNA is designated SEQ ID:21709, and is provided hereinbelow with reference to the sequence listing part.

[11201] VGAM803 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM803 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM803 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11202] VGAM803 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM803 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM803 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM803 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM803 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11203] The complementary binding of VGAM803 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM803 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM803 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM803 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11204] It is appreciated that VGAM803 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM803 host target genes. The mRNA of each one of this plurality of VGAM803 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM803 RNA, herein designated VGAM RNA, and which when bound by VGAM803 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM803 host target proteins.

[11205] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM803 gene, herein designated VGAM GENE, on one or more VGAM803 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11206] It is yet further appreciated that a function of VGAM803 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM803 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM803 correlate with, and may be deduced from, the identity of the host target genes which VGAM803 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11207] Nucleotide sequences of the VGAM803 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM803 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM803 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM803 are further described hereinbelow with reference to Table 1.

[11208] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM803 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11209] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 804 (VGAM804) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11210] VGAM804 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM804 was detected is described hereinabove with reference to Figs. 2-8.

[11211] VGAM804 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Feline foamy virus. VGAM804 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11212] VGAM804 gene, herein designated VGAM GENE, encodes a VGAM804 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM804 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM804 precursor RNA is designated SEQ ID:21718, and is provided hereinbelow with reference to the sequence listing part.

[11213] VGAM804 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM804 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11214] An enzyme complex designated DICER COMPLEX, dices the VGAM804 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM804 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM804 RNA is designated SEQ ID:21719, and is provided hereinbelow with reference to the sequence listing part.

[11215] VGAM804 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM804 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM804 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11216] VGAM804 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM804 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM804 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM804 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM804 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11217] The complementary binding of VGAM804 RNA, herein designated VGAM RNA, to host target binding sites on VGAM804 host target RNA, herein designated VGAM HOST



TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM804 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM804 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11218] It is appreciated that VGAM804 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM804 host target genes. The mRNA of each one of this plurality of VGAM804 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM804 RNA, herein designated VGAM RNA, and which when bound by VGAM804 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM804 host target proteins.

[11219] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM804 gene, herein designated VGAM GENE, on one or more VGAM804 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11220] It is yet further appreciated that a function of VGAM804 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM804 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM804 correlate with, and may be deduced from, the identity of the host target genes which VGAM804 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11221] Nucleotide sequences of the VGAM804 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM804 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM804 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM804 are further described hereinbelow with reference to Table 1.

[11222] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM804 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11223] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 805 (VGAM805) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11224] VGAM805 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM805 was detected is described hereinabove with reference to Figs. 2-8.

[11225] VGAM805 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus.

VGAM805 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11226] VGAM805 gene, herein designated VGAM GENE, encodes a VGAM805 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM805 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM805 precursor RNA is designated SEQ ID:21744, and is provided hereinbelow with reference to the sequence listing part.

[11227] VGAM805 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM805 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11228] An enzyme complex designated DICER COMPLEX, dices the VGAM805 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM805 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM805 RNA is designated SEQ ID:21745, and is provided hereinbelow with reference to the sequence listing part.

[11229] VGAM805 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM805 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM805 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11230] VGAM805 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM805 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM805 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM805 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM805 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11231] The complementary binding of VGAM805 RNA, herein designated VGAM RNA, to host target binding sites on VGAM805 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM805 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM805 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11232] It is appreciated that VGAM805 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM805 host target genes. The mRNA of each one of this plurality of VGAM805 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM805 RNA, herein designated VGAM RNA, and which when bound by VGAM805 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM805 host target proteins.

[11233] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM805 gene, herein designated VGAM GENE, on one or more VGAM805 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11234] It is yet further appreciated that a function of VGAM805 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM805 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM805 correlate with, and may be deduced from, the identity of the host target genes which VGAM805 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11235] Nucleotide sequences of the VGAM805 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM805 RNA, herein designated VGAM RNA, and a



schematic representation of the secondary folding of VGAM805 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM805 are further described hereinbelow with reference to Table 1.

[11236] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM805 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11237] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 806 (VGAM806) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11238] VGAM806 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM806 was detected is described hereinabove with reference to Figs. 2-8.

[11239] VGAM806 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus

type 7. VGAM806 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11240] VGAM806 gene, herein designated VGAM GENE, encodes a VGAM806 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM806 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM806 precursor RNA is designated SEQ ID:21764, and is provided hereinbelow with reference to the sequence listing part.

[11241] VGAM806 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM806 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11242] An enzyme complex designated DICER COMPLEX, dices

the VGAM806 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM806 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM806 RNA is designated SEQ ID:21765, and is provided hereinbelow with reference to the sequence listing part.

[11243] VGAM806 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM806 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM806 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11244] VGAM806 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM806 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM806 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM806 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM806 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11245] The complementary binding of VGAM806 RNA, herein designated VGAM RNA, to host target binding sites on VGAM806 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM806 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM806 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11246] It is appreciated that VGAM806 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM806 host target genes. The mRNA of each one of this plurality of VGAM806 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM806 RNA, herein designated VGAM RNA, and which when bound by VGAM806 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM806 host target proteins.

[11247] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM806 gene, herein designated VGAM GENE, on one or more VGAM806 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11248] It is yet further appreciated that a function of VGAM806 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM806 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 7. Specific functions, and accordingly utilities, of VGAM806 correlate with, and may be deduced from, the identity of the host target genes which VGAM806 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11249] Nucleotide sequences of the VGAM806 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM806 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM806 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM806 are further described hereinbelow with reference to Table 1.

[11250] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM806 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11251] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 807 (VGAM807) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11252] VGAM807 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM807 was detected is described hereinabove with reference to Figs. 2-8.

[11253] VGAM807 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cherry mottle leaf virus. VGAM807 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[11254] VGAM807 gene, herein designated VGAM GENE, encodes a VGAM807 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM807 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM807 precursor RNA is designated SEQ ID:21800, and is provided hereinbelow with reference to the sequence listing part.

[11255] VGAM807 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM807 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11256] An enzyme complex designated DICER COMPLEX, dices the VGAM807 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM807 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM807 RNA is designated SEQ ID:21801, and is provided hereinbelow with reference to the sequence listing part.

[11257] VGAM807 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM807 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM807 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11258] VGAM807 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM807 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM807 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM807 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM807 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11259] The complementary binding of VGAM807 RNA, herein designated VGAM RNA, to host target binding sites on VGAM807 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM807 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM807 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11260] It is appreciated that VGAM807 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM807 host target genes. The mRNA of each one of this plurality of VGAM807 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM807 RNA, herein designated VGAM RNA, and which when bound by VGAM807 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM807 host target proteins.

[11261] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM807 gene, herein designated VGAM GENE, on one or more VGAM807 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11262] It is yet further appreciated that a function of VGAM807 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM807 include diagnosis, prevention and treatment of viral infection by Cherry mottle leaf virus. Specific functions, and accordingly utilities, of VGAM807 correlate with, and may be deduced from, the identity of the host target genes which VGAM807 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11263] Nucleotide sequences of the VGAM807 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM807 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM807 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM807 are further described hereinbelow with reference to Table 1.

[11264] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM807 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11265] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 808 (VGAM808) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11266] VGAM808 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM808 was detected is described hereinabove with reference to Figs. 2-8.

[11267] VGAM808 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cherry mottle leaf virus. VGAM808 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[11268] VGAM808 gene, herein designated VGAM GENE, encodes a VGAM808 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM808 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM808 precursor RNA is designated SEQ ID:21815, and is provided hereinbelow with reference to the sequence listing part.

[11269] VGAM808 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM808 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11270] An enzyme complex designated DICER COMPLEX, dices the VGAM808 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM808 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM808 RNA is designated SEQ ID:21816, and is provided hereinbelow with reference to the sequence listing part.

[11271] VGAM808 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM808 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM808 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11272] VGAM808 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM808 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM808 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM808 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM808 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11273] The complementary binding of VGAM808 RNA, herein designated VGAM RNA, to host target binding sites on VGAM808 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM808 host target RNA, herein designated VGAM HOST TARGET RNA,



into VGAM808 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11274] It is appreciated that VGAM808 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM808 host target genes. The mRNA of each one of this plurality of VGAM808 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM808 RNA, herein designated VGAM RNA, and which when bound by VGAM808 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM808 host target proteins.

[11275] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM808 gene, herein designated VGAM GENE, on one or more VGAM808 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11276] It is yet further appreciated that a function of VGAM808 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM808 include diagnosis, prevention and treatment of viral infection by Cherry mottle leaf virus. Specific functions, and accordingly utilities, of VGAM808 correlate with, and may be deduced from, the identity of the host target genes which VGAM808 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11277] Nucleotide sequences of the VGAM808 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM808 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM808 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM808 are further de-

scribed hereinbelow with reference to Table 1.

[11278] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM808 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11279] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 809 (VGAM809) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11280] VGAM809 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM809 was detected is described hereinabove with reference to Figs. 2-8.

[11281] VGAM809 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cherry mottle leaf virus. VGAM809 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11282] VGAM809 gene, herein designated VGAM GENE, encodes a VGAM809 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM809 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM809 precursor RNA is designated SEQ ID:21824, and is provided hereinbelow with reference to the sequence listing part.

[11283] VGAM809 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM809 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11284] An enzyme complex designated DICER COMPLEX, dices the VGAM809 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM809 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM809 RNA is designated SEQ ID:21825, and is provided hereinbelow with reference to the sequence listing part.

[11285] VGAM809 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM809 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM809 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11286] VGAM809 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM809 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM809 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM809 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM809 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11287] The complementary binding of VGAM809 RNA, herein designated VGAM RNA, to host target binding sites on VGAM809 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM809 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM809 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11288] It is appreciated that VGAM809 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM809 host target genes. The mRNA of each one of this plurality of VGAM809 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM809 RNA, herein designated VGAM RNA, and which when bound by VGAM809 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM809 host target proteins.

[11289] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM809 gene, herein designated VGAM GENE, on one or more VGAM809 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11290] It is yet further appreciated that a function of VGAM809 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM809 include diagnosis, prevention and treatment of viral infection by Cherry mottle leaf virus. Specific functions, and accordingly utilities, of VGAM809 correlate with, and may be deduced from, the identity of the host target genes which VGAM809 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11291] Nucleotide sequences of the VGAM809 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM809 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM809 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM809 are further described hereinbelow with reference to Table 1.



[11292] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM809 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11293] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 810 (VGAM810) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11294] VGAM810 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM810 was detected is described hereinabove with reference to Figs. 2-8.

[11295] VGAM810 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM810 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11296] VGAM810 gene, herein designated VGAM GENE, encodes a

VGAM810 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM810 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM810 precursor RNA is designated SEQ ID:21923, and is provided hereinbelow with reference to the sequence listing part.

[11297] VGAM810 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM810 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11298] An enzyme complex designated DICER COMPLEX, dices the VGAM810 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM810 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM810 RNA is designated SEQ ID:21924, and is provided hereinbelow with reference to the sequence listing part.

[11299] VGAM810 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM810 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM810 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11300] VGAM810 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM810 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM810 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM810 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM810 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11301] The complementary binding of VGAM810 RNA, herein designated VGAM RNA, to host target binding sites on VGAM810 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM810 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM810 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[11302] It is appreciated that VGAM810 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM810 host target genes. The mRNA of each one of this plurality of VGAM810 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM810 RNA, herein designated VGAM RNA, and which when bound by VGAM810 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM810 host target proteins.

[11303] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM810 gene, herein designated VGAM GENE, on one or more VGAM810 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11304] It is yet further appreciated that a function of VGAM810 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM810 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM810 correlate with, and may be deduced from, the identity of the host target genes which VGAM810 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11305] Nucleotide sequences of the VGAM810 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM810 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM810 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM810 are further described hereinbelow with reference to Table 1.

[11306] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM810 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11307] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 811 (VGAM811) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11308] VGAM811 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM811 was detected is described hereinabove with reference to Figs. 2-8.

[11309] VGAM811 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM811 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11310] VGAM811 gene, herein designated VGAM GENE, encodes a VGAM811 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM811 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM811 precursor RNA is designated SEQ ID:21939, and is provided hereinbelow with reference to the sequence listing part.

[11311] VGAM811 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM811 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11312] An enzyme complex designated DICER COMPLEX, dices the VGAM811 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM811 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM811 RNA is designated SEQ ID:21940, and is provided hereinbelow with reference to the sequence listing part.

[11313] VGAM811 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM811 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM811 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11314] VGAM811 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM811 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM811 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM811 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM811 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11315] The complementary binding of VGAM811 RNA, herein designated VGAM RNA, to host target binding sites on VGAM811 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM811 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM811 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11316] It is appreciated that VGAM811 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM811 host target genes. The mRNA of each one of this plurality of VGAM811 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM811 RNA, herein designated VGAM RNA, and which when bound by VGAM811 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM811 host target proteins.

[11317] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM811 gene, herein designated VGAM GENE, on one or more VGAM811 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11318] It is yet further appreciated that a function of VGAM811 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM811 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM811 correlate with, and may be deduced from, the identity of the host target genes which VGAM811 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11319] Nucleotide sequences of the VGAM811 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM811 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM811 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM811 are further described hereinbelow with reference to Table 1.

[11320] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM811 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11321] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 812 (VGAM812) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11322] VGAM812 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM812 was detected is described hereinabove with reference to Figs. 2–8.

[11323] VGAM812 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM812 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11324] VGAM812 gene, herein designated VGAM GENE, encodes a VGAM812 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM812 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM812 precursor RNA is designated SEQ ID:21977, and is provided hereinbelow with reference to the sequence listing part.

[11325] VGAM812 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM812 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11326] An enzyme complex designated DICER COMPLEX, dices the VGAM812 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM812 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM812 RNA is designated SEQ ID:21978, and is provided hereinbelow with reference to the sequence listing part.

[11327] VGAM812 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM812 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM812 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11328] VGAM812 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM812 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM812 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM812 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM812 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11329] The complementary binding of VGAM812 RNA, herein designated VGAM RNA, to host target binding sites on VGAM812 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM812 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM812 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11330] It is appreciated that VGAM812 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM812 host target genes. The mRNA of each one of this plurality of VGAM812 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM812 RNA, herein designated VGAM RNA, and which when bound by VGAM812 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM812 host target proteins.

[11331] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM812 gene, herein designated VGAM GENE, on one or more VGAM812 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11332] It is yet further appreciated that a function of VGAM812 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM812 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM812 correlate with, and may be deduced from, the identity of the host target genes which VGAM812 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11333] Nucleotide sequences of the VGAM812 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM812 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM812 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM812 are further described hereinbelow with reference to Table 1.

[11334] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM812 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11335] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 813 (VGAM813) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11336] VGAM813 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM813 was detected is described hereinabove with reference to Figs. 2–8.

[11337] VGAM813 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM813 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11338] VGAM813 gene, herein designated VGAM GENE, encodes a VGAM813 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM813 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM813 precursor RNA is designated SEQ ID:21981, and is provided hereinbelow with reference to the sequence listing part.

[11339] VGAM813 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM813 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11340] An enzyme complex designated DICER COMPLEX, dices the VGAM813 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM813 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM813 RNA is designated SEQ ID:21982, and is provided hereinbelow with reference to the sequence listing part.

[11341] VGAM813 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM813 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM813 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11342] VGAM813 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM813 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM813 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM813 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM813 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11343] The complementary binding of VGAM813 RNA, herein designated VGAM RNA, to host target binding sites on VGAM813 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM813 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM813 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11344] It is appreciated that VGAM813 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM813 host target genes. The mRNA of each one of this plurality of VGAM813 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM813 RNA, herein designated VGAM RNA, and which when bound by VGAM813 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM813 host target proteins.

[11345] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM813 gene, herein designated VGAM GENE, on one or more VGAM813 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[11346] It is yet further appreciated that a function of VGAM813 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM813 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM813 correlate with, and may be deduced from, the identity of the host target genes which VGAM813 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11347] Nucleotide sequences of the VGAM813 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM813 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM813 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM813 are further described hereinbelow with reference to Table 1.

[11348] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM813 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11349] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 814 (VGAM814) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11350] VGAM814 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM814 was detected is described hereinabove with reference to Figs. 2–8.

[11351] VGAM814 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM814 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11352] VGAM814 gene, herein designated VGAM GENE, encodes a VGAM814 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM814 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM814 precursor RNA is designated SEQ ID:22006, and is provided hereinbelow with reference to the sequence listing part.

[11353] VGAM814 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM814 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11354] An enzyme complex designated DICER COMPLEX, dices the VGAM814 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM814 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM814 RNA is designated SEQ ID:22007, and is provided hereinbelow with reference to the sequence listing part.

[11355] VGAM814 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM814 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM814 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11356] VGAM814 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM814 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM814 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM814 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM814 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11357] The complementary binding of VGAM814 RNA, herein designated VGAM RNA, to host target binding sites on VGAM814 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM814 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM814 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11358] It is appreciated that VGAM814 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM814 host target genes. The mRNA of

each one of this plurality of VGAM814 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM814 RNA, herein designated VGAM RNA, and which when bound by VGAM814 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM814 host target proteins.

[11359] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM814 gene, herein designated VGAM GENE, on one or more VGAM814 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[11360] It is yet further appreciated that a function of VGAM814 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM814 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM814 correlate with, and may be deduced from, the identity of the host target genes which VGAM814 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11361] Nucleotide sequences of the VGAM814 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM814 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM814 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM814 are further described hereinbelow with reference to Table 1.

[11362] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM814 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[11363] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 815 (VGAM815) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11364] VGAM815 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM815 was detected is described hereinabove with reference to Figs. 2–8.

[11365] VGAM815 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM815 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11366] VGAM815 gene, herein designated VGAM GENE, encodes a VGAM815 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM815 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM815 precursor RNA is designated SEQ ID:22019, and is provided hereinbelow with reference to the sequence listing part.

[11367] VGAM815 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM815 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11368] An enzyme complex designated DICER COMPLEX, dices the VGAM815 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM815 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM815 RNA is designated SEQ ID:22020, and



is provided hereinbelow with reference to the sequence listing part.

[11369] VGAM815 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM815 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM815 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11370] VGAM815 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM815 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM815 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM815 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM815 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11371] The complementary binding of VGAM815 RNA, herein designated VGAM RNA, to host target binding sites on VGAM815 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM815 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM815 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11372] It is appreciated that VGAM815 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM815 host target genes. The mRNA of each one of this plurality of VGAM815 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM815 RNA, herein designated VGAM RNA, and which when bound by VGAM815 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM815 host target proteins.

[11373] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM815 gene, herein designated VGAM GENE, on one or more VGAM815 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11374] It is yet further appreciated that a function of VGAM815 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM815 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM815 correlate with, and may be deduced from, the identity of the host target genes which VGAM815 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11375] Nucleotide sequences of the VGAM815 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM815 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM815 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM815 are further described hereinbelow with reference to Table 1.

[11376] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM815 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11377] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 816 (VGAM816) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11378] VGAM816 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM816 was detected is described hereinabove with reference to Figs. 2–8.

[11379] VGAM816 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM816 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11380] VGAM816 gene, herein designated VGAM GENE, encodes a VGAM816 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM816 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM816 precursor RNA is

designated SEQ ID:22026, and is provided hereinbelow with reference to the sequence listing part.

[11381] VGAM816 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM816 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11382] An enzyme complex designated DICER COMPLEX, dices the VGAM816 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM816 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM816 RNA is designated SEQ ID:22027, and is provided hereinbelow with reference to the sequence

listing part.

[11383] VGAM816 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM816 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM816 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11384] VGAM816 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM816 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM816 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM816 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM816 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11385] The complementary binding of VGAM816 RNA, herein designated VGAM RNA, to host target binding sites on VGAM816 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM816 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM816 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11386] It is appreciated that VGAM816 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM816 host target genes. The mRNA of each one of this plurality of VGAM816 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM816 RNA, herein designated VGAM RNA, and which when bound by VGAM816 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM816 host target proteins.

[11387] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM816 gene, herein designated VGAM GENE, on one or more VGAM816 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11388] It is yet further appreciated that a function of VGAM816 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM816 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM816 correlate with, and may be deduced from, the identity of the host target genes which VGAM816 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11389] Nucleotide sequences of the VGAM816 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM816 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM816 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM816 are further described hereinbelow with reference to Table 1.

[11390] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM816 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11391] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 817 (VGAM817) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11392] VGAM817 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM817 was detected is described hereinabove with reference to Figs. 2–8.

[11393] VGAM817 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM817 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11394] VGAM817 gene, herein designated VGAM GENE, encodes a VGAM817 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM817 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM817 precursor RNA is designated SEQ ID:22048, and is provided hereinbelow

with reference to the sequence listing part.

[11395] VGAM817 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM817 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11396] An enzyme complex designated DICER COMPLEX, dices the VGAM817 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM817 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM817 RNA is designated SEQ ID:22049, and is provided hereinbelow with reference to the sequence listing part.

[11397] VGAM817 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM817 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM817 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11398] VGAM817 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM817 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM817 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM817 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM817 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11399] The complementary binding of VGAM817 RNA, herein designated VGAM RNA, to host target binding sites on VGAM817 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM817 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM817 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11400] It is appreciated that VGAM817 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM817 host target genes. The mRNA of each one of this plurality of VGAM817 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM817 RNA, herein designated VGAM RNA, and which when bound by VGAM817 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM817 host target proteins.

[11401] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM817 gene, herein designated VGAM GENE, on one or more VGAM817 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11402] It is yet further appreciated that a function of VGAM817 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM817 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM817 correlate with, and may be deduced from, the identity of the host target genes which VGAM817 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11403] Nucleotide sequences of the VGAM817 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM817 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM817 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM817 are further described hereinbelow with reference to Table 1.

[11404] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM817 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11405] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 818 (VGAM818) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11406] VGAM818 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM818 was detected is described hereinabove with reference to Figs. 2–8.

[11407] VGAM818 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sugarcane yellow leaf virus. VGAM818 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11408] VGAM818 gene, herein designated VGAM GENE, encodes a VGAM818 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM818 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM818 precursor RNA is designated SEQ ID:22054, and is provided hereinbelow with reference to the sequence listing part.

[11409] VGAM818 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM818 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11410] An enzyme complex designated DICER COMPLEX, dices the VGAM818 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM818 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM818 RNA is designated SEQ ID:22055, and is provided hereinbelow with reference to the sequence listing part.

[11411] VGAM818 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM818 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM818 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11412] VGAM818 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM818 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM818 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM818 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM818 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11413] The complementary binding of VGAM818 RNA, herein designated VGAM RNA, to host target binding sites on VGAM818 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM818 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM818 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11414] It is appreciated that VGAM818 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM818 host target genes. The mRNA of each one of this plurality of VGAM818 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM818 RNA, herein designated VGAM

RNA, and which when bound by VGAM818 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM818 host target proteins.

[11415] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM818 gene, herein designated VGAM GENE, on one or more VGAM818 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11416] It is yet further appreciated that a function of VGAM818 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM818 include diagnosis, prevention and treatment of viral infection by Sugarcane yellow leaf virus. Specific functions, and accordingly utilities, of VGAM818 correlate with, and may be deduced from, the identity of the host target genes which VGAM818 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11417] Nucleotide sequences of the VGAM818 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM818 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM818 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM818 are further described hereinbelow with reference to Table 1.

[11418] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM818 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11419] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 819 (VGAM819) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11420] VGAM819 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM819 was detected is described hereinabove with reference to Figs. 2–8.

[11421] VGAM819 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sugarcane yellow leaf virus. VGAM819 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11422] VGAM819 gene, herein designated VGAM GENE, encodes a VGAM819 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM819 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM819 precursor RNA is designated SEQ ID:22189, and is provided hereinbelow with reference to the sequence listing part.

[11423] VGAM819 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM819 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11424] An enzyme complex designated DICER COMPLEX, dices the VGAM819 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM819 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM819 RNA is designated SEQ ID:22190, and is provided hereinbelow with reference to the sequence listing part.

[11425] VGAM819 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM819 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM819 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11426] VGAM819 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM819 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM819 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM819 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM819 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11427] The complementary binding of VGAM819 RNA, herein designated VGAM RNA, to host target binding sites on VGAM819 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM819 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM819 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11428] It is appreciated that VGAM819 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM819 host target genes. The mRNA of each one of this plurality of VGAM819 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM819 RNA, herein designated VGAM RNA, and which when bound by VGAM819 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM819 host target proteins.

[11429] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM819 gene, herein designated VGAM GENE, on one or more VGAM819 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11430] It is yet further appreciated that a function of VGAM819 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM819 include diagnosis, prevention and

treatment of viral infection by Sugarcane yellow leaf virus. Specific functions, and accordingly utilities, of VGAM819 correlate with, and may be deduced from, the identity of the host target genes which VGAM819 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11431] Nucleotide sequences of the VGAM819 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM819 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM819 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM819 are further described hereinbelow with reference to Table 1.

[11432] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM819 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11433] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 820 (VGAM820) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11434] VGAM820 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM820 was detected is described hereinabove with reference to Figs. 2–8.

[11435] VGAM820 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sugarcane yellow leaf virus. VGAM820 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11436] VGAM820 gene, herein designated VGAM GENE, encodes a VGAM820 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM820 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM820 precursor RNA is designated SEQ ID:22217, and is provided hereinbelow with reference to the sequence listing part.

[11437] VGAM820 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM820 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11438] An enzyme complex designated DICER COMPLEX, dices the VGAM820 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM820 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM820 RNA is designated SEQ ID:22218, and is provided hereinbelow with reference to the sequence listing part.

[11439] VGAM820 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM820 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM820 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11440] VGAM820 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM820 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM820 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM820 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM820 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11441] The complementary binding of VGAM820 RNA, herein designated VGAM RNA, to host target binding sites on VGAM820 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM820 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM820 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11442] It is appreciated that VGAM820 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM820 host target genes. The mRNA of each one of this plurality of VGAM820 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM820 RNA, herein designated VGAM RNA, and which when bound by VGAM820 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM820 host target proteins.

[11443] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM820 gene, herein designated VGAM GENE, on one or more VGAM820 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11444] It is yet further appreciated that a function of VGAM820 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM820 include diagnosis, prevention and treatment of viral infection by Sugarcane yellow leaf virus.

Specific functions, and accordingly utilities, of VGAM820 correlate with, and may be deduced from, the identity of the host target genes which VGAM820 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11445] Nucleotide sequences of the VGAM820 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM820 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM820 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM820 are further described hereinbelow with reference to Table 1.

[11446] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM820 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11447] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 821 (VGAM821) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[11448] VGAM821 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM821 was detected is described hereinabove with reference to Figs. 2–8.

[11449] VGAM821 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM821 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11450] VGAM821 gene, herein designated VGAM GENE, encodes a VGAM821 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM821 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM821 precursor RNA is designated SEQ ID:22258, and is provided hereinbelow with reference to the sequence listing part.

[11451] VGAM821 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM821 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11452] An enzyme complex designated DICER COMPLEX, dices the VGAM821 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM821 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM821 RNA is designated SEQ ID:22259, and is provided hereinbelow with reference to the sequence listing part.

[11453] VGAM821 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM821 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM821 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11454] VGAM821 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM821 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM821 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM821 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM821 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11455] The complementary binding of VGAM821 RNA, herein designated VGAM RNA, to host target binding sites on VGAM821 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM821 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM821 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11456] It is appreciated that VGAM821 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM821 host target genes. The mRNA of each one of this plurality of VGAM821 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM821 RNA, herein designated VGAM RNA, and which when bound by VGAM821 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM821 host target proteins.

[11457] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM821 gene, herein designated VGAM GENE, on one or more VGAM821 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11458] It is yet further appreciated that a function of VGAM821 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM821 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM821 correlate with, and may be deduced from, the identity of the host

target genes which VGAM821 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11459] Nucleotide sequences of the VGAM821 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM821 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM821 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM821 are further described hereinbelow with reference to Table 1.

[11460] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM821 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11461] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 822 (VGAM822) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[11462] VGAM822 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM822 was detected is described hereinabove with reference to Figs. 2–8.

[11463] VGAM822 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM822 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11464] VGAM822 gene, herein designated VGAM GENE, encodes a VGAM822 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM822 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM822 precursor RNA is designated SEQ ID:22265, and is provided hereinbelow with reference to the sequence listing part.

[11465] VGAM822 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM822 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11466] An enzyme complex designated DICER COMPLEX, dices the VGAM822 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM822 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM822 RNA is designated SEQ ID:22266, and is provided hereinbelow with reference to the sequence listing part.

[11467] VGAM822 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM822 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM822 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11468] VGAM822 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM822 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM822 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM822 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM822 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11469] The complementary binding of VGAM822 RNA, herein designated VGAM RNA, to host target binding sites on VGAM822 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM822 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM822 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11470] It is appreciated that VGAM822 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM822 host target genes. The mRNA of each one of this plurality of VGAM822 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM822 RNA, herein designated VGAM RNA, and which when bound by VGAM822 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM822 host target proteins.

[11471] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM822 gene, herein designated VGAM GENE, on one or more VGAM822 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11472] It is yet further appreciated that a function of VGAM822 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM822 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM822 correlate with, and may be deduced from, the identity of the host target genes which VGAM822 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[11473] Nucleotide sequences of the VGAM822 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM822 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM822 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM822 are further described hereinbelow with reference to Table 1.

[11474] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM822 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11475] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 823 (VGAM823) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11476] VGAM823 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM823 was detected is described hereinabove with reference to Figs. 2–8.

[11477] VGAM823 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM823 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11478] VGAM823 gene, herein designated VGAM GENE, encodes a VGAM823 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM823 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM823 precursor RNA is designated SEQ ID:22279, and is provided hereinbelow with reference to the sequence listing part.

[11479] VGAM823 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM823 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11480] An enzyme complex designated DICER COMPLEX, dices the VGAM823 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM823 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM823 RNA is designated SEQ ID:22280, and is provided hereinbelow with reference to the sequence listing part.

[11481] VGAM823 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM823 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM823 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11482] VGAM823 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM823 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM823 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM823 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM823 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[11483] The complementary binding of VGAM823 RNA, herein designated VGAM RNA, to host target binding sites on VGAM823 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM823 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM823 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11484] It is appreciated that VGAM823 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM823 host target genes. The mRNA of each one of this plurality of VGAM823 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM823 RNA, herein designated VGAM RNA, and which when bound by VGAM823 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM823 host target proteins.

[11485] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM823 gene, herein designated VGAM GENE, on one or more VGAM823 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11486] It is yet further appreciated that a function of VGAM823 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM823 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM823 correlate with, and may be deduced from, the identity of the host target genes which VGAM823 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[11487] Nucleotide sequences of the VGAM823 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM823 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM823 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM823 are further described hereinbelow with reference to Table 1.

[11488] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM823 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11489] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 824 (VGAM824) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11490] VGAM824 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM824 was detected is described hereinabove with reference to Figs. 2–8.

[11491] VGAM824 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6.

VGAM824 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11492] VGAM824 gene, herein designated VGAM GENE, encodes a VGAM824 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM824 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM824 precursor RNA is designated SEQ ID:22295, and is provided hereinbelow with reference to the sequence listing part.

[11493] VGAM824 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM824 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11494] An enzyme complex designated DICER COMPLEX, dices the VGAM824 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM824 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM824 RNA is designated SEQ ID:22296, and is provided hereinbelow with reference to the sequence listing part.

[11495] VGAM824 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM824 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM824 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[11496] VGAM824 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM824 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM824 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM824 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM824 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11497] The complementary binding of VGAM824 RNA, herein designated VGAM RNA, to host target binding sites on VGAM824 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM824 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM824 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11498] It is appreciated that VGAM824 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM824 host target genes. The mRNA of each one of this plurality of VGAM824 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM824 RNA, herein designated VGAM RNA, and which when bound by VGAM824 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM824 host target proteins.

[11499] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM824 gene, herein designated VGAM GENE, on one or



more VGAM824 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11500] It is yet further appreciated that a function of VGAM824 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM824 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM824 correlate with, and may be deduced from, the identity of the host target genes which VGAM824 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11501] Nucleotide sequences of the VGAM824 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM824 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM824 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM824 are further described hereinbelow with reference to Table 1.

[11502] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM824 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11503] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 825 (VGAM825) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11504] VGAM825 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM825 was detected is described

hereinabove with reference to Figs. 2–8.

[11505] VGAM825 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM825 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11506] VGAM825 gene, herein designated VGAM GENE, encodes a VGAM825 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM825 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM825 precursor RNA is designated SEQ ID:22338, and is provided hereinbelow with reference to the sequence listing part.

[11507] VGAM825 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM825 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11508] An enzyme complex designated DICER COMPLEX, dices the VGAM825 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM825 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM825 RNA is designated SEQ ID:22339, and is provided hereinbelow with reference to the sequence listing part.

[11509] VGAM825 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM825 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM825 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11510] VGAM825 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM825 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM825 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM825 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM825 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11511] The complementary binding of VGAM825 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM825 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM825 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM825 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11512] It is appreciated that VGAM825 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM825 host target genes. The mRNA of each one of this plurality of VGAM825 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM825 RNA, herein designated VGAM RNA, and which when bound by VGAM825 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM825 host target proteins.

[11513] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM825 gene, herein designated VGAM GENE, on one or more VGAM825 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11514] It is yet further appreciated that a function of VGAM825 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM825 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM825 correlate with, and may be deduced from, the identity of the host target genes which VGAM825 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11515] Nucleotide sequences of the VGAM825 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM825 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM825 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM825 are further described hereinbelow with reference to Table 1.

[11516] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM825 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11517] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 826 (VGAM826) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11518] VGAM826 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM826 was detected is described hereinabove with reference to Figs. 2-8.



[11519] VGAM826 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM826 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11520] VGAM826 gene, herein designated VGAM GENE, encodes a VGAM826 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM826 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM826 precursor RNA is designated SEQ ID:22356, and is provided hereinbelow with reference to the sequence listing part.

[11521] VGAM826 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM826 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[11522] An enzyme complex designated DICER COMPLEX, dices the VGAM826 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM826 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM826 RNA is designated SEQ ID:22357, and is provided hereinbelow with reference to the sequence listing part.

[11523] VGAM826 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM826 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM826 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11524] VGAM826 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM826 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM826 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM826 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM826 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11525] The complementary binding of VGAM826 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM826 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM826 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM826 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11526] It is appreciated that VGAM826 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM826 host target genes. The mRNA of each one of this plurality of VGAM826 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM826 RNA, herein designated VGAM RNA, and which when bound by VGAM826 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM826 host target proteins.

[11527] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM826 gene, herein designated VGAM GENE, on one or more VGAM826 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11528] It is yet further appreciated that a function of VGAM826 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM826 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM826 correlate with, and may be deduced from, the identity of the host target genes which VGAM826 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11529] Nucleotide sequences of the VGAM826 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM826 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM826 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM826 are further described hereinbelow with reference to Table 1.

[11530] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM826 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11531] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 827 (VGAM827) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11532] VGAM827 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM827 was detected is described hereinabove with reference to Figs. 2-8.

[11533] VGAM827 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 6. VGAM827 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11534] VGAM827 gene, herein designated VGAM GENE, encodes a VGAM827 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM827 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM827 precursor RNA is designated SEQ ID:22364, and is provided hereinbelow with reference to the sequence listing part.

[11535] VGAM827 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM827 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11536] An enzyme complex designated DICER COMPLEX, dices the VGAM827 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM827 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM827 RNA is designated SEQ ID:22365, and is provided hereinbelow with reference to the sequence listing part.

[11537] VGAM827 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM827 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM827 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11538] VGAM827 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM827 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM827 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM827 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM827 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11539] The complementary binding of VGAM827 RNA, herein designated VGAM RNA, to host target binding sites on VGAM827 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM827 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM827 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11540] It is appreciated that VGAM827 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM827 host target genes. The mRNA of each one of this plurality of VGAM827 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM827 RNA, herein designated VGAM RNA, and which when bound by VGAM827 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM827 host target proteins.

[11541] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM827 gene, herein designated VGAM GENE, on one or more VGAM827 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11542] It is yet further appreciated that a function of VGAM827 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM827 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM827 correlate with, and may be deduced from, the identity of the host target genes which VGAM827 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11543] Nucleotide sequences of the VGAM827 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM827 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM827 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM827 are further described hereinbelow with reference to Table 1.

[11544] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM827 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11545] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 828 (VGAM828) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11546] VGAM828 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM828 was detected is described hereinabove with reference to Figs. 2-8.

[11547] VGAM828 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus.

VGAM828 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11548] VGAM828 gene, herein designated VGAM GENE, encodes a VGAM828 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM828 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM828 precursor RNA is designated SEQ ID:22396, and is provided hereinbelow with reference to the sequence listing part.

[11549] VGAM828 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM828 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11550] An enzyme complex designated DICER COMPLEX, dices

the VGAM828 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM828 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM828 RNA is designated SEQ ID:22397, and is provided hereinbelow with reference to the sequence listing part.

[11551] VGAM828 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM828 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM828 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11552] VGAM828 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM828 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM828 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM828 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM828 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11553] The complementary binding of VGAM828 RNA, herein designated VGAM RNA, to host target binding sites on VGAM828 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM828 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM828 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11554] It is appreciated that VGAM828 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM828 host target genes. The mRNA of each one of this plurality of VGAM828 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM828 RNA, herein designated VGAM RNA, and which when bound by VGAM828 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM828 host target proteins.

[11555] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM828 gene, herein designated VGAM GENE, on one or more VGAM828 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11556] It is yet further appreciated that a function of VGAM828 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM828 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM828 correlate with, and may be deduced from, the identity of the host target genes which VGAM828 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11557] Nucleotide sequences of the VGAM828 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM828 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM828 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM828 are further described hereinbelow with reference to Table 1.

[11558] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM828 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11559] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 829 (VGAM829) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11560] VGAM829 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM829 was detected is described hereinabove with reference to Figs. 2-8.

[11561] VGAM829 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM829 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[11562] VGAM829 gene, herein designated VGAM GENE, encodes a VGAM829 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM829 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM829 precursor RNA is designated SEQ ID:22414, and is provided hereinbelow with reference to the sequence listing part.

[11563] VGAM829 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM829 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11564] An enzyme complex designated DICER COMPLEX, dices the VGAM829 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM829 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM829 RNA is designated SEQ ID:22415, and is provided hereinbelow with reference to the sequence listing part.

[11565] VGAM829 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM829 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM829 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11566] VGAM829 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM829 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM829 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM829 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM829 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11567] The complementary binding of VGAM829 RNA, herein designated VGAM RNA, to host target binding sites on VGAM829 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM829 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM829 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11568] It is appreciated that VGAM829 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM829 host target genes. The mRNA of each one of this plurality of VGAM829 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM829 RNA, herein designated VGAM RNA, and which when bound by VGAM829 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM829 host target proteins.

[11569] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM829 gene, herein designated VGAM GENE, on one or more VGAM829 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11570] It is yet further appreciated that a function of VGAM829 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM829 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM829 correlate with, and may be deduced from, the identity of the host target genes which VGAM829 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11571] Nucleotide sequences of the VGAM829 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM829 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM829 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM829 are further described hereinbelow with reference to Table 1.

[11572] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM829 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11573] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 830 (VGAM830) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11574] VGAM830 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM830 was detected is described hereinabove with reference to Figs. 2-8.

[11575] VGAM830 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM830 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[11576] VGAM830 gene, herein designated VGAM GENE, encodes a VGAM830 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM830 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM830 precursor RNA is designated SEQ ID:22420, and is provided hereinbelow with reference to the sequence listing part.

[11577] VGAM830 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM830 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11578] An enzyme complex designated DICER COMPLEX, dices the VGAM830 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM830 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM830 RNA is designated SEQ ID:22421, and is provided hereinbelow with reference to the sequence listing part.

[11579] VGAM830 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM830 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM830 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11580] VGAM830 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM830 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM830 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM830 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM830 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11581] The complementary binding of VGAM830 RNA, herein designated VGAM RNA, to host target binding sites on VGAM830 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM830 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM830 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11582] It is appreciated that VGAM830 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM830 host target genes. The mRNA of each one of this plurality of VGAM830 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM830 RNA, herein designated VGAM RNA, and which when bound by VGAM830 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM830 host target proteins.

[11583] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM830 gene, herein designated VGAM GENE, on one or more VGAM830 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11584] It is yet further appreciated that a function of VGAM830 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM830 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM830 correlate with, and may be deduced from, the identity of the host target genes which VGAM830 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11585] Nucleotide sequences of the VGAM830 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM830 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM830 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM830 are further de-

scribed hereinbelow with reference to Table 1.

[11586] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM830 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11587] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 831 (VGAM831) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11588] VGAM831 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM831 was detected is described hereinabove with reference to Figs. 2-8.

[11589] VGAM831 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM831 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11590] VGAM831 gene, herein designated VGAM GENE, encodes a VGAM831 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM831 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM831 precursor RNA is designated SEQ ID:22429, and is provided hereinbelow with reference to the sequence listing part.

[11591] VGAM831 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM831 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11592] An enzyme complex designated DICER COMPLEX, dices the VGAM831 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM831 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM831 RNA is designated SEQ ID:22430, and is provided hereinbelow with reference to the sequence listing part.

[11593] VGAM831 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM831 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM831 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11594] VGAM831 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM831 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM831 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM831 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM831 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11595] The complementary binding of VGAM831 RNA, herein designated VGAM RNA, to host target binding sites on VGAM831 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM831 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM831 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11596] It is appreciated that VGAM831 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM831 host target genes. The mRNA of each one of this plurality of VGAM831 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM831 RNA, herein designated VGAM RNA, and which when bound by VGAM831 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM831 host target proteins.

[11597] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM831 gene, herein designated VGAM GENE, on one or more VGAM831 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11598] It is yet further appreciated that a function of VGAM831 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM831 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM831 correlate with, and may be deduced from, the identity of the host target genes which VGAM831 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11599] Nucleotide sequences of the VGAM831 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM831 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM831 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM831 are further described hereinbelow with reference to Table 1.

[11600] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM831 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11601] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 832 (VGAM832) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11602] VGAM832 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM832 was detected is described hereinabove with reference to Figs. 2-8.

[11603] VGAM832 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM832 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11604] VGAM832 gene, herein designated VGAM GENE, encodes a

VGAM832 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM832 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM832 precursor RNA is designated SEQ ID:22439, and is provided hereinbelow with reference to the sequence listing part.

[11605] VGAM832 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM832 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11606] An enzyme complex designated DICER COMPLEX, dices the VGAM832 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM832 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM832 RNA is designated SEQ ID:22440, and is provided hereinbelow with reference to the sequence listing part.

[11607] VGAM832 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM832 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM832 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11608] VGAM832 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM832 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM832 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM832 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM832 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11609] The complementary binding of VGAM832 RNA, herein designated VGAM RNA, to host target binding sites on VGAM832 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM832 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM832 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[11610] It is appreciated that VGAM832 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM832 host target genes. The mRNA of each one of this plurality of VGAM832 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM832 RNA, herein designated VGAM RNA, and which when bound by VGAM832 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM832 host target proteins.

[11611] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM832 gene, herein designated VGAM GENE, on one or more VGAM832 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11612] It is yet further appreciated that a function of VGAM832 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM832 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM832 correlate with, and may be deduced from, the identity of the host target genes which VGAM832 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11613] Nucleotide sequences of the VGAM832 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM832 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM832 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM832 are further described hereinbelow with reference to Table 1.

[11614] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM832 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11615] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 833 (VGAM833) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11616] VGAM833 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM833 was detected is described hereinabove with reference to Figs. 2-8.

[11617] VGAM833 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal yellow dwarf virus-RPV. VGAM833 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11618] VGAM833 gene, herein designated VGAM GENE, encodes a VGAM833 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM833 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM833 precursor RNA is designated SEQ ID:22447, and is provided hereinbelow with reference to the sequence listing part.

[11619] VGAM833 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM833 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11620] An enzyme complex designated DICER COMPLEX, dices the VGAM833 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM833 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM833 RNA is designated SEQ ID:22448, and is provided hereinbelow with reference to the sequence listing part.

[11621] VGAM833 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM833 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM833 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11622] VGAM833 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM833 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM833 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM833 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM833 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11623] The complementary binding of VGAM833 RNA, herein designated VGAM RNA, to host target binding sites on VGAM833 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM833 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM833 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11624] It is appreciated that VGAM833 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM833 host target genes. The mRNA of each one of this plurality of VGAM833 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM833 RNA, herein designated VGAM RNA, and which when bound by VGAM833 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM833 host target proteins.

[11625] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM833 gene, herein designated VGAM GENE, on one or more VGAM833 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11626] It is yet further appreciated that a function of VGAM833 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM833 include diagnosis, prevention and treatment of viral infection by Cereal yellow dwarf virus–RPV. Specific functions, and accordingly utilities, of VGAM833 correlate with, and may be deduced from, the identity of the host target genes which VGAM833 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11627] Nucleotide sequences of the VGAM833 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM833 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM833 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM833 are further described hereinbelow with reference to Table 1.

[11628] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM833 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11629] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 834 (VGAM834) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11630] VGAM834 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM834 was detected is described hereinabove with reference to Figs. 2–8.

[11631] VGAM834 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM834 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11632] VGAM834 gene, herein designated VGAM GENE, encodes a VGAM834 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike



most ordinary genes, VGAM834 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM834 precursor RNA is designated SEQ ID:22459, and is provided hereinbelow with reference to the sequence listing part.

[11633] VGAM834 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM834 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11634] An enzyme complex designated DICER COMPLEX, dices the VGAM834 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM834 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM834 RNA is designated SEQ ID:22460, and is provided hereinbelow with reference to the sequence listing part.

[11635] VGAM834 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM834 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM834 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11636] VGAM834 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM834 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM834 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM834 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM834 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11637] The complementary binding of VGAM834 RNA, herein designated VGAM RNA, to host target binding sites on VGAM834 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM834 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM834 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11638] It is appreciated that VGAM834 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM834 host target genes. The mRNA of each one of this plurality of VGAM834 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM834 RNA, herein designated VGAM RNA, and which when bound by VGAM834 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM834 host target proteins.

[11639] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM834 gene, herein designated VGAM GENE, on one or more VGAM834 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11640] It is yet further appreciated that a function of VGAM834 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM834 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM834 correlate with, and may be deduced from, the identity of the host target genes which VGAM834 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11641] Nucleotide sequences of the VGAM834 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM834 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM834 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM834 are further described hereinbelow with reference to Table 1.

[11642] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM834 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11643] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 835 (VGAM835) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11644] VGAM835 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM835 was detected is described hereinabove with reference to Figs. 2–8.

[11645] VGAM835 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal yellow dwarf virus–RPV. VGAM835 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11646] VGAM835 gene, herein designated VGAM GENE, encodes a VGAM835 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM835 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM835 precursor RNA is designated SEQ ID:22473, and is provided hereinbelow with reference to the sequence listing part.

[11647] VGAM835 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM835 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11648] An enzyme complex designated DICER COMPLEX, dices the VGAM835 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM835 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 75%) nucleotide sequence of VGAM835 RNA is designated SEQ ID:22474, and is provided hereinbelow with reference to the sequence listing part.

[11649] VGAM835 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM835 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM835 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11650] VGAM835 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM835 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM835 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM835 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM835 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11651] The complementary binding of VGAM835 RNA, herein designated VGAM RNA, to host target binding sites on VGAM835 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM835 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM835 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11652] It is appreciated that VGAM835 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM835 host target genes. The mRNA of each one of this plurality of VGAM835 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM835 RNA, herein designated VGAM RNA, and which when bound by VGAM835 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM835 host target proteins.

[11653] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM835 gene, herein designated VGAM GENE, on one or more VGAM835 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [11654] It is yet further appreciated that a function of VGAM835 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM835 include diagnosis, prevention and treatment of viral infection by Cereal yellow dwarf virus–RPV. Specific functions, and accordingly utilities, of VGAM835 correlate with, and may be deduced from, the identity of the host target genes which VGAM835 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [11655] Nucleotide sequences of the VGAM835 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM835 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM835 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM835 are further described hereinbelow with reference to Table 1.
- [11656] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM835 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11657] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 836 (VGAM836) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11658] VGAM836 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM836 was detected is described hereinabove with reference to Figs. 2–8.

[11659] VGAM836 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal yellow dwarf virus–RPV. VGAM836 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11660] VGAM836 gene, herein designated VGAM GENE, encodes a VGAM836 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM836 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM836 precursor RNA is designated SEQ ID:22483, and is provided hereinbelow with reference to the sequence listing part.

[11661] VGAM836 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM836 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11662] An enzyme complex designated DICER COMPLEX, dices the VGAM836 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM836 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM836 RNA is designated SEQ ID:22484, and is provided hereinbelow with reference to the sequence listing part.

[11663] VGAM836 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM836 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM836 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11664] VGAM836 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM836 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM836 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM836 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM836 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11665] The complementary binding of VGAM836 RNA, herein designated VGAM RNA, to host target binding sites on VGAM836 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM836 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM836 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11666] It is appreciated that VGAM836 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM836 host target genes. The mRNA of

each one of this plurality of VGAM836 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM836 RNA, herein designated VGAM RNA, and which when bound by VGAM836 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM836 host target proteins.

[11667] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM836 gene, herein designated VGAM GENE, on one or more VGAM836 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[11668] It is yet further appreciated that a function of VGAM836 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM836 include diagnosis, prevention and treatment of viral infection by Cereal yellow dwarf virus–RPV. Specific functions, and accordingly utilities, of VGAM836 correlate with, and may be deduced from, the identity of the host target genes which VGAM836 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11669] Nucleotide sequences of the VGAM836 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM836 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM836 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM836 are further described hereinbelow with reference to Table 1.

[11670] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM836 RNA, herein designated VGAM RNA, are de–

scribed hereinbelow with reference to Table 2.

[11671] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 837 (VGAM837) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11672] VGAM837 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM837 was detected is described hereinabove with reference to Figs. 2–8.

[11673] VGAM837 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola virus. VGAM837 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11674] VGAM837 gene, herein designated VGAM GENE, encodes a VGAM837 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM837 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM837 precursor RNA is

designated SEQ ID:22491, and is provided hereinbelow with reference to the sequence listing part.

[11675] VGAM837 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM837 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11676] An enzyme complex designated DICER COMPLEX, dices the VGAM837 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM837 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM837 RNA is designated SEQ ID:22492, and is provided hereinbelow with reference to the sequence

listing part.

[11677] VGAM837 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM837 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM837 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11678] VGAM837 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM837 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM837 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM837 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM837 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11679] The complementary binding of VGAM837 RNA, herein designated VGAM RNA, to host target binding sites on VGAM837 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM837 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM837 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11680] It is appreciated that VGAM837 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM837 host target genes. The mRNA of each one of this plurality of VGAM837 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM837 RNA, herein designated VGAM RNA, and which when bound by VGAM837 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM837 host target proteins.

[11681] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM837 gene, herein designated VGAM GENE, on one or more VGAM837 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11682] It is yet further appreciated that a function of VGAM837 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM837 include diagnosis, prevention and treatment of viral infection by Variola virus. Specific functions, and accordingly utilities, of VGAM837 correlate with, and may be deduced from, the identity of the host target genes which VGAM837 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11683] Nucleotide sequences of the VGAM837 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM837 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM837 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM837 are further described hereinbelow with reference to Table 1.

[11684] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM837 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11685] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 838 (VGAM838) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11686] VGAM838 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM838 was detected is described hereinabove with reference to Figs. 2–8.

[11687] VGAM838 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal yellow dwarf virus–RPV. VGAM838 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11688] VGAM838 gene, herein designated VGAM GENE, encodes a VGAM838 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM838 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM838 precursor RNA is designated SEQ ID:22494, and is provided hereinbelow



with reference to the sequence listing part.

[11689] VGAM838 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM838 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11690] An enzyme complex designated DICER COMPLEX, dices the VGAM838 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM838 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM838 RNA is designated SEQ ID:22495, and is provided hereinbelow with reference to the sequence listing part.

[11691] VGAM838 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM838 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM838 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11692] VGAM838 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM838 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM838 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM838 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM838 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11693] The complementary binding of VGAM838 RNA, herein designated VGAM RNA, to host target binding sites on VGAM838 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM838 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM838 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11694] It is appreciated that VGAM838 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM838 host target genes. The mRNA of each one of this plurality of VGAM838 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM838 RNA, herein designated VGAM RNA, and which when bound by VGAM838 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM838 host target proteins.

[11695] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM838 gene, herein designated VGAM GENE, on one or more VGAM838 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11696] It is yet further appreciated that a function of VGAM838 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM838 include diagnosis, prevention and treatment of viral infection by Cereal yellow dwarf virus–RPV. Specific functions, and accordingly utilities, of VGAM838 correlate with, and may be deduced from, the identity of the host target genes which VGAM838 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11697] Nucleotide sequences of the VGAM838 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM838 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM838 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM838 are further described hereinbelow with reference to Table 1.

[11698] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM838 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11699] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 839 (VGAM839) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11700] VGAM839 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM839 was detected is described hereinabove with reference to Figs. 2–8.

[11701] VGAM839 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal yellow dwarf virus–RPV. VGAM839 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11702] VGAM839 gene, herein designated VGAM GENE, encodes a VGAM839 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM839 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM839 precursor RNA is designated SEQ ID:22501, and is provided hereinbelow with reference to the sequence listing part.

[11703] VGAM839 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM839 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11704] An enzyme complex designated DICER COMPLEX, dices the VGAM839 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM839 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM839 RNA is designated SEQ ID:22502, and is provided hereinbelow with reference to the sequence listing part.

[11705] VGAM839 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM839 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM839 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11706] VGAM839 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM839 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM839 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM839 RNA, herein designated VGAM RNA, may have a different number of host target



binding sites in untranslated regions of a VGAM839 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11707] The complementary binding of VGAM839 RNA, herein designated VGAM RNA, to host target binding sites on VGAM839 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM839 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM839 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11708] It is appreciated that VGAM839 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM839 host target genes. The mRNA of each one of this plurality of VGAM839 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM839 RNA, herein designated VGAM

RNA, and which when bound by VGAM839 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM839 host target proteins.

[11709] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM839 gene, herein designated VGAM GENE, on one or more VGAM839 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11710] It is yet further appreciated that a function of VGAM839 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM839 include diagnosis, prevention and treatment of viral infection by Cereal yellow dwarf virus–RPV. Specific functions, and accordingly utilities, of VGAM839 correlate with, and may be deduced from, the identity of the host target genes which VGAM839 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11711] Nucleotide sequences of the VGAM839 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM839 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM839 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM839 are further described hereinbelow with reference to Table 1.

[11712] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM839 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11713] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes–

senger 840 (VGAM840) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11714] VGAM840 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM840 was detected is described hereinabove with reference to Figs. 2–8.

[11715] VGAM840 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal yellow dwarf virus–RPV. VGAM840 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11716] VGAM840 gene, herein designated VGAM GENE, encodes a VGAM840 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM840 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM840 precursor RNA is designated SEQ ID:22536, and is provided hereinbelow with reference to the sequence listing part.

[11717] VGAM840 precursor RNA, herein designated VGAM PRE–

CURSOR RNA, folds onto itself, forming VGAM840 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11718] An enzyme complex designated DICER COMPLEX, dices the VGAM840 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM840 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM840 RNA is designated SEQ ID:22537, and is provided hereinbelow with reference to the sequence listing part.

[11719] VGAM840 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM840 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM840 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11720] VGAM840 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM840 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM840 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM840 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM840 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11721] The complementary binding of VGAM840 RNA, herein designated VGAM RNA, to host target binding sites on VGAM840 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM840 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM840 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11722] It is appreciated that VGAM840 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM840 host target genes. The mRNA of each one of this plurality of VGAM840 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM840 RNA, herein designated VGAM RNA, and which when bound by VGAM840 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM840 host target proteins.

[11723] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM840 gene, herein designated VGAM GENE, on one or more VGAM840 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11724] It is yet further appreciated that a function of VGAM840 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM840 include diagnosis, prevention and



treatment of viral infection by Cereal yellow dwarf virus–RPV. Specific functions, and accordingly utilities, of VGAM840 correlate with, and may be deduced from, the identity of the host target genes which VGAM840 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11725] Nucleotide sequences of the VGAM840 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM840 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM840 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM840 are further described hereinbelow with reference to Table 1.

[11726] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM840 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11727] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 841 (VGAM841) viral gene, which modulates ex–

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11728] VGAM841 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM841 was detected is described hereinabove with reference to Figs. 2–8.

[11729] VGAM841 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal yellow dwarf virus–RPV. VGAM841 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11730] VGAM841 gene, herein designated VGAM GENE, encodes a VGAM841 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM841 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM841 precursor RNA is designated SEQ ID:22541, and is provided hereinbelow with reference to the sequence listing part.

[11731] VGAM841 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM841 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11732] An enzyme complex designated DICER COMPLEX, dices the VGAM841 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM841 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM841 RNA is designated SEQ ID:22542, and is provided hereinbelow with reference to the sequence listing part.

[11733] VGAM841 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM841 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM841 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11734] VGAM841 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM841 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM841 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM841 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM841 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11735] The complementary binding of VGAM841 RNA, herein designated VGAM RNA, to host target binding sites on VGAM841 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM841 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM841 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11736] It is appreciated that VGAM841 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM841 host target genes. The mRNA of each one of this plurality of VGAM841 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM841 RNA, herein designated VGAM RNA, and which when bound by VGAM841 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM841 host target proteins.

[11737] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM841 gene, herein designated VGAM GENE, on one or more VGAM841 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11738] It is yet further appreciated that a function of VGAM841 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM841 include diagnosis, prevention and treatment of viral infection by Cereal yellow dwarf virus–

RPV. Specific functions, and accordingly utilities, of VGAM841 correlate with, and may be deduced from, the identity of the host target genes which VGAM841 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11739] Nucleotide sequences of the VGAM841 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM841 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM841 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM841 are further described hereinbelow with reference to Table 1.

[11740] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM841 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11741] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 842 (VGAM842) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[11742] VGAM842 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM842 was detected is described hereinabove with reference to Figs. 2–8.

[11743] VGAM842 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine rhinitis B virus. VGAM842 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11744] VGAM842 gene, herein designated VGAM GENE, encodes a VGAM842 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM842 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM842 precursor RNA is designated SEQ ID:22552, and is provided hereinbelow with reference to the sequence listing part.

[11745] VGAM842 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM842 folded precursor RNA, herein designated VGAM FOLDED PRECUR-



SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11746] An enzyme complex designated DICER COMPLEX, dices the VGAM842 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM842 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM842 RNA is designated SEQ ID:22553, and is provided hereinbelow with reference to the sequence listing part.

[11747] VGAM842 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM842 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM842 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11748] VGAM842 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM842 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM842 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM842 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM842 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11749] The complementary binding of VGAM842 RNA, herein designated VGAM RNA, to host target binding sites on VGAM842 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM842 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM842 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11750] It is appreciated that VGAM842 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM842 host target genes. The mRNA of each one of this plurality of VGAM842 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM842 RNA, herein designated VGAM RNA, and which when bound by VGAM842 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM842 host target proteins.

[11751] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM842 gene, herein designated VGAM GENE, on one or more VGAM842 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11752] It is yet further appreciated that a function of VGAM842 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM842 include diagnosis, prevention and treatment of viral infection by Equine rhinitis B virus. Specific functions, and accordingly utilities, of VGAM842 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM842 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11753] Nucleotide sequences of the VGAM842 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM842 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM842 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM842 are further described hereinbelow with reference to Table 1.

[11754] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM842 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11755] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 843 (VGAM843) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[11756] VGAM843 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM843 was detected is described hereinabove with reference to Figs. 2–8.

[11757] VGAM843 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM843 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11758] VGAM843 gene, herein designated VGAM GENE, encodes a VGAM843 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM843 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM843 precursor RNA is designated SEQ ID:22573, and is provided hereinbelow with reference to the sequence listing part.

[11759] VGAM843 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM843 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11760] An enzyme complex designated DICER COMPLEX, dices the VGAM843 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM843 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM843 RNA is designated SEQ ID:22574, and is provided hereinbelow with reference to the sequence listing part.

[11761] VGAM843 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM843 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM843 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11762] VGAM843 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM843 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM843 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM843 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM843 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an



example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11763] The complementary binding of VGAM843 RNA, herein designated VGAM RNA, to host target binding sites on VGAM843 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM843 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM843 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11764] It is appreciated that VGAM843 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM843 host target genes. The mRNA of each one of this plurality of VGAM843 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM843 RNA, herein designated VGAM RNA, and which when bound by VGAM843 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM843 host target proteins.

[11765] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM843 gene, herein designated VGAM GENE, on one or more VGAM843 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11766] It is yet further appreciated that a function of VGAM843 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM843 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM843 correlate with, and may be deduced from, the identity of

the host target genes which VGAM843 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11767] Nucleotide sequences of the VGAM843 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM843 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM843 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM843 are further described hereinbelow with reference to Table 1.

[11768] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM843 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11769] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 844 (VGAM844) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11770] VGAM844 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM844 was detected is described hereinabove with reference to Figs. 2–8.

[11771] VGAM844 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM844 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11772] VGAM844 gene, herein designated VGAM GENE, encodes a VGAM844 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM844 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM844 precursor RNA is designated SEQ ID:22579, and is provided hereinbelow with reference to the sequence listing part.

[11773] VGAM844 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM844 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11774] An enzyme complex designated DICER COMPLEX, dices the VGAM844 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM844 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM844 RNA is designated SEQ ID:22580, and is provided hereinbelow with reference to the sequence listing part.

[11775] VGAM844 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM844 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM844 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11776] VGAM844 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM844 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM844 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM844 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM844 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11777] The complementary binding of VGAM844 RNA, herein designated VGAM RNA, to host target binding sites on VGAM844 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM844 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM844 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11778] It is appreciated that VGAM844 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM844 host target genes. The mRNA of each one of this plurality of VGAM844 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM844 RNA, herein designated VGAM RNA, and which when bound by VGAM844 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM844 host target proteins.

[11779] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM844 gene, herein designated VGAM GENE, on one or more VGAM844 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11780] It is yet further appreciated that a function of VGAM844 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM844 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM844 correlate with, and may be deduced from, the identity of the host target genes which VGAM844 binds and inhibits, and



the function of these host target genes, as elaborated hereinbelow.

[11781] Nucleotide sequences of the VGAM844 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM844 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM844 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM844 are further described hereinbelow with reference to Table 1.

[11782] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM844 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11783] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 845 (VGAM845) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11784] VGAM845 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM845 was detected is described hereinabove with reference to Figs. 2–8.

[11785] VGAM845 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM845 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11786] VGAM845 gene, herein designated VGAM GENE, encodes a VGAM845 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM845 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM845 precursor RNA is designated SEQ ID:22587, and is provided hereinbelow with reference to the sequence listing part.

[11787] VGAM845 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM845 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11788] An enzyme complex designated DICER COMPLEX, dices the VGAM845 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM845 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM845 RNA is designated SEQ ID:22588, and is provided hereinbelow with reference to the sequence listing part.

[11789] VGAM845 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM845 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM845 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11790] VGAM845 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM845 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM845 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM845 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM845 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[11791] The complementary binding of VGAM845 RNA, herein designated VGAM RNA, to host target binding sites on VGAM845 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM845 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM845 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11792] It is appreciated that VGAM845 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM845 host target genes. The mRNA of each one of this plurality of VGAM845 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM845 RNA, herein designated VGAM RNA, and which when bound by VGAM845 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM845 host target proteins.

[11793] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM845 gene, herein designated VGAM GENE, on one or more VGAM845 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11794] It is yet further appreciated that a function of VGAM845 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM845 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM845 correlate with, and may be deduced from, the identity of the host target genes which VGAM845 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[11795] Nucleotide sequences of the VGAM845 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM845 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM845 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM845 are further described hereinbelow with reference to Table 1.

[11796] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM845 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11797] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 846 (VGAM846) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11798] VGAM846 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM846 was detected is described hereinabove with reference to Figs. 2–8.

[11799] VGAM846 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM846 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11800] VGAM846 gene, herein designated VGAM GENE, encodes a VGAM846 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM846 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM846 precursor RNA is designated SEQ ID:22596, and is provided hereinbelow with reference to the sequence listing part.

[11801] VGAM846 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM846 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the



RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11802] An enzyme complex designated DICER COMPLEX, dices the VGAM846 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM846 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM846 RNA is designated SEQ ID:22597, and is provided hereinbelow with reference to the sequence listing part.

[11803] VGAM846 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM846 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM846 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[11804] VGAM846 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM846 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM846 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM846 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM846 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11805] The complementary binding of VGAM846 RNA, herein designated VGAM RNA, to host target binding sites on VGAM846 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM846 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM846 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11806] It is appreciated that VGAM846 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM846 host target genes. The mRNA of each one of this plurality of VGAM846 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM846 RNA, herein designated VGAM RNA, and which when bound by VGAM846 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM846 host target proteins.

[11807] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM846 gene, herein designated VGAM GENE, on one or

more VGAM846 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11808] It is yet further appreciated that a function of VGAM846 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM846 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM846 correlate with, and may be deduced from, the identity of the host target genes which VGAM846 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11809] Nucleotide sequences of the VGAM846 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM846 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM846 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM846 are further described hereinbelow with reference to Table 1.

[11810] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM846 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11811] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 847 (VGAM847) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11812] VGAM847 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM847 was detected is described

hereinabove with reference to Figs. 2–8.

[11813] VGAM847 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM847 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11814] VGAM847 gene, herein designated VGAM GENE, encodes a VGAM847 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM847 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM847 precursor RNA is designated SEQ ID:22610, and is provided hereinbelow with reference to the sequence listing part.

[11815] VGAM847 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM847 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11816] An enzyme complex designated DICER COMPLEX, dices the VGAM847 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM847 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM847 RNA is designated SEQ ID:22611, and is provided hereinbelow with reference to the sequence listing part.

[11817] VGAM847 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM847 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM847 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11818] VGAM847 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM847 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM847 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM847 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM847 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11819] The complementary binding of VGAM847 RNA, herein



designated VGAM RNA, to host target binding sites on VGAM847 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM847 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM847 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11820] It is appreciated that VGAM847 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM847 host target genes. The mRNA of each one of this plurality of VGAM847 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM847 RNA, herein designated VGAM RNA, and which when bound by VGAM847 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM847 host target proteins.

[11821] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM847 gene, herein designated VGAM GENE, on one or more VGAM847 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11822] It is yet further appreciated that a function of VGAM847 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM847 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM847 correlate with, and may be deduced from, the identity of the host target genes which VGAM847 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11823] Nucleotide sequences of the VGAM847 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the dived VGAM847 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM847 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM847 are further described hereinbelow with reference to Table 1.

[11824] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM847 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11825] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 848 (VGAM848) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11826] VGAM848 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM848 was detected is described hereinabove with reference to Figs. 2-8.

[11827] VGAM848 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM848 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11828] VGAM848 gene, herein designated VGAM GENE, encodes a VGAM848 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM848 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM848 precursor RNA is designated SEQ ID:22677, and is provided hereinbelow with reference to the sequence listing part.

[11829] VGAM848 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM848 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[11830] An enzyme complex designated DICER COMPLEX, dices the VGAM848 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM848 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM848 RNA is designated SEQ ID:22678, and is provided hereinbelow with reference to the sequence listing part.

[11831] VGAM848 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM848 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM848 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11832] VGAM848 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM848 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM848 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM848 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM848 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11833] The complementary binding of VGAM848 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM848 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM848 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM848 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11834] It is appreciated that VGAM848 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM848 host target genes. The mRNA of each one of this plurality of VGAM848 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM848 RNA, herein designated VGAM RNA, and which when bound by VGAM848 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM848 host target proteins.

[11835] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM848 gene, herein designated VGAM GENE, on one or more VGAM848 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11836] It is yet further appreciated that a function of VGAM848 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM848 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM848 correlate with, and may be deduced from, the identity of the host target genes which VGAM848 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11837] Nucleotide sequences of the VGAM848 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



diced VGAM848 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM848 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM848 are further described hereinbelow with reference to Table 1.

[11838] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM848 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11839] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 849 (VGAM849) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11840] VGAM849 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM849 was detected is described hereinabove with reference to Figs. 2-8.

[11841] VGAM849 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Monkeypox virus.

VGAM849 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11842] VGAM849 gene, herein designated VGAM GENE, encodes a VGAM849 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM849 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM849 precursor RNA is designated SEQ ID:22715, and is provided hereinbelow with reference to the sequence listing part.

[11843] VGAM849 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM849 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11844] An enzyme complex designated DICER COMPLEX, dices the VGAM849 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM849 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM849 RNA is designated SEQ ID:22716, and is provided hereinbelow with reference to the sequence listing part.

[11845] VGAM849 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM849 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM849 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11846] VGAM849 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM849 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM849 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM849 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM849 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11847] The complementary binding of VGAM849 RNA, herein designated VGAM RNA, to host target binding sites on VGAM849 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM849 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM849 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11848] It is appreciated that VGAM849 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM849 host target genes. The mRNA of each one of this plurality of VGAM849 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM849 RNA, herein designated VGAM RNA, and which when bound by VGAM849 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM849 host target proteins.

[11849] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM849 gene, herein designated VGAM GENE, on one or more VGAM849 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11850] It is yet further appreciated that a function of VGAM849 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM849 include diagnosis, prevention and treatment of viral infection by Monkeypox virus. Specific functions, and accordingly utilities, of VGAM849 correlate with, and may be deduced from, the identity of the host target genes which VGAM849 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11851] Nucleotide sequences of the VGAM849 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM849 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM849 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM849 are further described hereinbelow with reference to Table 1.

[11852] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM849 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11853] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 850 (VGAM850) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11854] VGAM850 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM850 was detected is described hereinabove with reference to Figs. 2-8.

[11855] VGAM850 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3.

VGAM850 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11856] VGAM850 gene, herein designated VGAM GENE, encodes a VGAM850 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM850 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM850 precursor RNA is designated SEQ ID:22743, and is provided hereinbelow with reference to the sequence listing part.

[11857] VGAM850 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM850 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11858] An enzyme complex designated DICER COMPLEX, dices



the VGAM850 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM850 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM850 RNA is designated SEQ ID:22744, and is provided hereinbelow with reference to the sequence listing part.

[11859] VGAM850 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM850 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM850 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11860] VGAM850 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM850 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM850 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM850 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM850 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11861] The complementary binding of VGAM850 RNA, herein designated VGAM RNA, to host target binding sites on VGAM850 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM850 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM850 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11862] It is appreciated that VGAM850 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM850 host target genes. The mRNA of each one of this plurality of VGAM850 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM850 RNA, herein designated VGAM RNA, and which when bound by VGAM850 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM850 host target proteins.

[11863] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM850 gene, herein designated VGAM GENE, on one or more VGAM850 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11864] It is yet further appreciated that a function of VGAM850 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM850 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM850 correlate with, and may be deduced from, the identity of the host target genes which VGAM850 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11865] Nucleotide sequences of the VGAM850 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM850 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM850 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM850 are further described hereinbelow with reference to Table 1.

[11866] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM850 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11867] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 851 (VGAM851) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11868] VGAM851 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM851 was detected is described hereinabove with reference to Figs. 2-8.

[11869] VGAM851 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM851 host target gene, herein designated VGAM HOST TARGET

GENE, is a human gene contained in the human genome.

[11870] VGAM851 gene, herein designated VGAM GENE, encodes a VGAM851 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM851 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM851 precursor RNA is designated SEQ ID:22834, and is provided hereinbelow with reference to the sequence listing part.

[11871] VGAM851 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM851 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11872] An enzyme complex designated DICER COMPLEX, dices the VGAM851 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM851 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM851 RNA is designated SEQ ID:22835, and is provided hereinbelow with reference to the sequence listing part.

[11873] VGAM851 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM851 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM851 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11874] VGAM851 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM851 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM851 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM851 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM851 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11875] The complementary binding of VGAM851 RNA, herein designated VGAM RNA, to host target binding sites on VGAM851 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM851 host target RNA, herein designated VGAM HOST TARGET RNA,



into VGAM851 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11876] It is appreciated that VGAM851 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM851 host target genes. The mRNA of each one of this plurality of VGAM851 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM851 RNA, herein designated VGAM RNA, and which when bound by VGAM851 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM851 host target proteins.

[11877] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM851 gene, herein designated VGAM GENE, on one or more VGAM851 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11878] It is yet further appreciated that a function of VGAM851 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM851 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM851 correlate with, and may be deduced from, the identity of the host target genes which VGAM851 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11879] Nucleotide sequences of the VGAM851 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM851 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM851 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM851 are further de-

scribed hereinbelow with reference to Table 1.

[11880] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM851 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11881] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 852 (VGAM852) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11882] VGAM852 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM852 was detected is described hereinabove with reference to Figs. 2-8.

[11883] VGAM852 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 10. VGAM852 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11884] VGAM852 gene, herein designated VGAM GENE, encodes a VGAM852 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM852 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM852 precursor RNA is designated SEQ ID:22848, and is provided hereinbelow with reference to the sequence listing part.

[11885] VGAM852 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM852 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11886] An enzyme complex designated DICER COMPLEX, dices the VGAM852 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM852 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM852 RNA is designated SEQ ID:22849, and is provided hereinbelow with reference to the sequence listing part.

[11887] VGAM852 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM852 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM852 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11888] VGAM852 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM852 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM852 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM852 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM852 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11889] The complementary binding of VGAM852 RNA, herein designated VGAM RNA, to host target binding sites on VGAM852 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM852 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM852 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11890] It is appreciated that VGAM852 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM852 host target genes. The mRNA of each one of this plurality of VGAM852 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM852 RNA, herein designated VGAM RNA, and which when bound by VGAM852 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM852 host target proteins.

[11891] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM852 gene, herein designated VGAM GENE, on one or more VGAM852 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11892] It is yet further appreciated that a function of VGAM852 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM852 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 10. Specific functions, and accordingly utilities, of VGAM852 correlate with, and may be deduced from, the identity of the host target genes which VGAM852 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11893] Nucleotide sequences of the VGAM852 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM852 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM852 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM852 are further described hereinbelow with reference to Table 1.



[11894] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM852 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11895] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 853 (VGAM853) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11896] VGAM853 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM853 was detected is described hereinabove with reference to Figs. 2-8.

[11897] VGAM853 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 10. VGAM853 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11898] VGAM853 gene, herein designated VGAM GENE, encodes a

VGAM853 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM853 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM853 precursor RNA is designated SEQ ID:22887, and is provided hereinbelow with reference to the sequence listing part.

[11899] VGAM853 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM853 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11900] An enzyme complex designated DICER COMPLEX, dices the VGAM853 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM853 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM853 RNA is designated SEQ ID:22888, and is provided hereinbelow with reference to the sequence listing part.

[11901] VGAM853 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM853 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM853 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11902] VGAM853 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM853 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM853 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM853 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM853 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11903] The complementary binding of VGAM853 RNA, herein designated VGAM RNA, to host target binding sites on VGAM853 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM853 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM853 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[11904] It is appreciated that VGAM853 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM853 host target genes. The mRNA of each one of this plurality of VGAM853 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM853 RNA, herein designated VGAM RNA, and which when bound by VGAM853 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM853 host target proteins.

[11905] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM853 gene, herein designated VGAM GENE, on one or more VGAM853 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11906] It is yet further appreciated that a function of VGAM853 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM853 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 10. Specific functions, and accordingly utilities, of VGAM853 correlate with, and may be deduced from, the identity of the host target genes which VGAM853 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11907] Nucleotide sequences of the VGAM853 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM853 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM853 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM853 are further described hereinbelow with reference to Table 1.

[11908] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM853 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11909] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 854 (VGAM854) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11910] VGAM854 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM854 was detected is described hereinabove with reference to Figs. 2-8.

[11911] VGAM854 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM854 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11912] VGAM854 gene, herein designated VGAM GENE, encodes a VGAM854 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM854 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM854 precursor RNA is designated SEQ ID:22911, and is provided hereinbelow with reference to the sequence listing part.

[11913] VGAM854 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM854 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11914] An enzyme complex designated DICER COMPLEX, dices the VGAM854 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM854 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM854 RNA is designated SEQ ID:22912, and is provided hereinbelow with reference to the sequence listing part.

[11915] VGAM854 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM854 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM854 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11916] VGAM854 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM854 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM854 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM854 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM854 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11917] The complementary binding of VGAM854 RNA, herein designated VGAM RNA, to host target binding sites on VGAM854 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM854 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM854 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11918] It is appreciated that VGAM854 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM854 host target genes. The mRNA of each one of this plurality of VGAM854 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM854 RNA, herein designated VGAM RNA, and which when bound by VGAM854 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM854 host target proteins.

[11919] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM854 gene, herein designated VGAM GENE, on one or more VGAM854 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11920] It is yet further appreciated that a function of VGAM854 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM854 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM854 correlate with, and may be deduced from, the identity of the host target genes which VGAM854 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11921] Nucleotide sequences of the VGAM854 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM854 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM854 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM854 are further described hereinbelow with reference to Table 1.

[11922] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM854 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11923] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 855 (VGAM855) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11924] VGAM855 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM855 was detected is described hereinabove with reference to Figs. 2–8.

[11925] VGAM855 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM855 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11926] VGAM855 gene, herein designated VGAM GENE, encodes a VGAM855 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM855 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM855 precursor RNA is designated SEQ ID:22923, and is provided hereinbelow with reference to the sequence listing part.

[11927] VGAM855 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM855 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11928] An enzyme complex designated DICER COMPLEX, dices the VGAM855 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM855 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM855 RNA is designated SEQ ID:22924, and is provided hereinbelow with reference to the sequence listing part.

[11929] VGAM855 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM855 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM855 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11930] VGAM855 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM855 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM855 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM855 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM855 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11931] The complementary binding of VGAM855 RNA, herein designated VGAM RNA, to host target binding sites on VGAM855 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM855 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM855 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11932] It is appreciated that VGAM855 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM855 host target genes. The mRNA of each one of this plurality of VGAM855 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM855 RNA, herein designated VGAM RNA, and which when bound by VGAM855 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM855 host target proteins.

[11933] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM855 gene, herein designated VGAM GENE, on one or more VGAM855 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11934] It is yet further appreciated that a function of VGAM855 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM855 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM855 correlate with, and may be deduced from, the identity of the host target genes which VGAM855 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11935] Nucleotide sequences of the VGAM855 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM855 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM855 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM855 are further described hereinbelow with reference to Table 1.

[11936] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM855 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11937] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 856 (VGAM856) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11938] VGAM856 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM856 was detected is described hereinabove with reference to Figs. 2–8.

[11939] VGAM856 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM856 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11940] VGAM856 gene, herein designated VGAM GENE, encodes a VGAM856 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM856 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM856 precursor RNA is designated SEQ ID:22935, and is provided hereinbelow with reference to the sequence listing part.

[11941] VGAM856 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM856 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11942] An enzyme complex designated DICER COMPLEX, dices the VGAM856 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM856 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM856 RNA is designated SEQ ID:22936, and is provided hereinbelow with reference to the sequence listing part.

[11943] VGAM856 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM856 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM856 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11944] VGAM856 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM856 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM856 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM856 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM856 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11945] The complementary binding of VGAM856 RNA, herein designated VGAM RNA, to host target binding sites on VGAM856 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM856 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM856 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11946] It is appreciated that VGAM856 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM856 host target genes. The mRNA of each one of this plurality of VGAM856 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM856 RNA, herein designated VGAM RNA, and which when bound by VGAM856 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM856 host target proteins.

[11947] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM856 gene, herein designated VGAM GENE, on one or more VGAM856 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[11948] It is yet further appreciated that a function of VGAM856 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM856 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM856 correlate with, and may be deduced from, the identity of the host target genes which VGAM856 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11949] Nucleotide sequences of the VGAM856 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM856 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM856 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM856 are further described hereinbelow with reference to Table 1.

[11950] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM856 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11951] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 857 (VGAM857) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11952] VGAM857 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM857 was detected is described hereinabove with reference to Figs. 2-8.

[11953] VGAM857 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM857 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11954] VGAM857 gene, herein designated VGAM GENE, encodes a VGAM857 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM857 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM857 precursor RNA is designated SEQ ID:22967, and is provided hereinbelow with reference to the sequence listing part.

[11955] VGAM857 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM857 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11956] An enzyme complex designated DICER COMPLEX, dices the VGAM857 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM857 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM857 RNA is designated SEQ ID:22968, and is provided hereinbelow with reference to the sequence listing part.

[11957] VGAM857 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM857 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM857 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11958] VGAM857 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM857 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM857 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM857 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM857 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11959] The complementary binding of VGAM857 RNA, herein designated VGAM RNA, to host target binding sites on VGAM857 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM857 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM857 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11960] It is appreciated that VGAM857 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM857 host target genes. The mRNA of

each one of this plurality of VGAM857 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM857 RNA, herein designated VGAM RNA, and which when bound by VGAM857 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM857 host target proteins.

[11961] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM857 gene, herein designated VGAM GENE, on one or more VGAM857 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[11962] It is yet further appreciated that a function of VGAM857 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM857 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM857 correlate with, and may be deduced from, the identity of the host target genes which VGAM857 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11963] Nucleotide sequences of the VGAM857 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM857 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM857 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM857 are further described hereinbelow with reference to Table 1.

[11964] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM857 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[11965] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 858 (VGAM858) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11966] VGAM858 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM858 was detected is described hereinabove with reference to Figs. 2–8.

[11967] VGAM858 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM858 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11968] VGAM858 gene, herein designated VGAM GENE, encodes a VGAM858 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM858 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM858 precursor RNA is designated SEQ ID:22979, and is provided hereinbelow with reference to the sequence listing part.

[11969] VGAM858 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM858 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11970] An enzyme complex designated DICER COMPLEX, dices the VGAM858 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM858 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM858 RNA is designated SEQ ID:22980, and



is provided hereinbelow with reference to the sequence listing part.

[11971] VGAM858 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM858 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM858 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11972] VGAM858 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM858 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM858 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM858 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM858 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11973] The complementary binding of VGAM858 RNA, herein designated VGAM RNA, to host target binding sites on VGAM858 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM858 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM858 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11974] It is appreciated that VGAM858 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM858 host target genes. The mRNA of each one of this plurality of VGAM858 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM858 RNA, herein designated VGAM RNA, and which when bound by VGAM858 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM858 host target proteins.

[11975] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM858 gene, herein designated VGAM GENE, on one or more VGAM858 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11976] It is yet further appreciated that a function of VGAM858 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM858 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM858 correlate with, and may be deduced from, the identity of the host target genes which VGAM858 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11977] Nucleotide sequences of the VGAM858 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM858 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM858 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM858 are further described hereinbelow with reference to Table 1.

[11978] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM858 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11979] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 859 (VGAM859) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11980] VGAM859 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM859 was detected is described hereinabove with reference to Figs. 2–8.

[11981] VGAM859 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM859 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11982] VGAM859 gene, herein designated VGAM GENE, encodes a VGAM859 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM859 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM859 precursor RNA is

designated SEQ ID:22988, and is provided hereinbelow with reference to the sequence listing part.

[11983] VGAM859 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM859 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11984] An enzyme complex designated DICER COMPLEX, dices the VGAM859 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM859 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM859 RNA is designated SEQ ID:22989, and is provided hereinbelow with reference to the sequence

listing part.

[11985] VGAM859 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM859 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM859 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[11986] VGAM859 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM859 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM859 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM859 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM859 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[11987] The complementary binding of VGAM859 RNA, herein designated VGAM RNA, to host target binding sites on VGAM859 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM859 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM859 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11988] It is appreciated that VGAM859 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM859 host target genes. The mRNA of each one of this plurality of VGAM859 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM859 RNA, herein designated VGAM RNA, and which when bound by VGAM859 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM859 host target proteins.

[11989] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM859 gene, herein designated VGAM GENE, on one or more VGAM859 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[11990] It is yet further appreciated that a function of VGAM859 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM859 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM859 correlate with, and may be deduced from, the identity of the host target genes which VGAM859 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11991] Nucleotide sequences of the VGAM859 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM859 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM859 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM859 are further described hereinbelow with reference to Table 1.

[11992] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM859 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11993] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 860 (VGAM860) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11994] VGAM860 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM860 was detected is described hereinabove with reference to Figs. 2–8.

[11995] VGAM860 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM860 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11996] VGAM860 gene, herein designated VGAM GENE, encodes a VGAM860 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM860 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM860 precursor RNA is designated SEQ ID:22995, and is provided hereinbelow

with reference to the sequence listing part.

[11997] VGAM860 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM860 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11998] An enzyme complex designated DICER COMPLEX, dices the VGAM860 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM860 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM860 RNA is designated SEQ ID:22996, and is provided hereinbelow with reference to the sequence listing part.

[11999] VGAM860 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM860 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM860 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12000] VGAM860 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM860 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM860 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM860 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM860 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12001] The complementary binding of VGAM860 RNA, herein designated VGAM RNA, to host target binding sites on VGAM860 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM860 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM860 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12002] It is appreciated that VGAM860 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM860 host target genes. The mRNA of each one of this plurality of VGAM860 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM860 RNA, herein designated VGAM RNA, and which when bound by VGAM860 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM860 host target proteins.

[12003] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM860 gene, herein designated VGAM GENE, on one or more VGAM860 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12004] It is yet further appreciated that a function of VGAM860 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM860 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM860 correlate with, and may be deduced from, the identity of the host target genes which VGAM860 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12005] Nucleotide sequences of the VGAM860 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM860 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM860 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM860 are further described hereinbelow with reference to Table 1.

[12006] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM860 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12007] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 861 (VGAM861) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12008] VGAM861 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM861 was detected is described hereinabove with reference to Figs. 2–8.

[12009] VGAM861 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM861 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12010] VGAM861 gene, herein designated VGAM GENE, encodes a VGAM861 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM861 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM861 precursor RNA is designated SEQ ID:23006, and is provided hereinbelow with reference to the sequence listing part.

[12011] VGAM861 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM861 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12012] An enzyme complex designated DICER COMPLEX, dices the VGAM861 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM861 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM861 RNA is designated SEQ ID:23007, and is provided hereinbelow with reference to the sequence listing part.

[12013] VGAM861 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM861 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM861 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12014] VGAM861 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM861 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM861 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM861 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM861 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12015] The complementary binding of VGAM861 RNA, herein designated VGAM RNA, to host target binding sites on VGAM861 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM861 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM861 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12016] It is appreciated that VGAM861 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM861 host target genes. The mRNA of each one of this plurality of VGAM861 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM861 RNA, herein designated VGAM

RNA, and which when bound by VGAM861 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM861 host target proteins.

[12017] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM861 gene, herein designated VGAM GENE, on one or more VGAM861 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12018] It is yet further appreciated that a function of VGAM861 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM861 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM861 correlate with, and may be deduced from, the identity of the host target genes which VGAM861 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12019] Nucleotide sequences of the VGAM861 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM861 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM861 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM861 are further described hereinbelow with reference to Table 1.

[12020] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM861 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12021] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 862 (VGAM862) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12022] VGAM862 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM862 was detected is described hereinabove with reference to Figs. 2–8.

[12023] VGAM862 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM862 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12024] VGAM862 gene, herein designated VGAM GENE, encodes a VGAM862 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM862 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM862 precursor RNA is designated SEQ ID:23094, and is provided hereinbelow with reference to the sequence listing part.

[12025] VGAM862 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM862 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12026] An enzyme complex designated DICER COMPLEX, dices the VGAM862 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM862 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM862 RNA is designated SEQ ID:23095, and is provided hereinbelow with reference to the sequence listing part.

[12027] VGAM862 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM862 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM862 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12028] VGAM862 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM862 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM862 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM862 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM862 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12029] The complementary binding of VGAM862 RNA, herein designated VGAM RNA, to host target binding sites on VGAM862 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM862 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM862 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12030] It is appreciated that VGAM862 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM862 host target genes. The mRNA of each one of this plurality of VGAM862 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM862 RNA, herein designated VGAM RNA, and which when bound by VGAM862 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM862 host target proteins.

[12031] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM862 gene, herein designated VGAM GENE, on one or more VGAM862 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12032] It is yet further appreciated that a function of VGAM862 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM862 include diagnosis, prevention and

treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM862 correlate with, and may be deduced from, the identity of the host target genes which VGAM862 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12033] Nucleotide sequences of the VGAM862 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM862 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM862 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM862 are further described hereinbelow with reference to Table 1.

[12034] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM862 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12035] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 863 (VGAM863) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12036] VGAM863 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM863 was detected is described hereinabove with reference to Figs. 2–8.

[12037] VGAM863 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM863 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12038] VGAM863 gene, herein designated VGAM GENE, encodes a VGAM863 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM863 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM863 precursor RNA is designated SEQ ID:23312, and is provided hereinbelow with reference to the sequence listing part.

[12039] VGAM863 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM863 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12040] An enzyme complex designated DICER COMPLEX, dices the VGAM863 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM863 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM863 RNA is designated SEQ ID:23313, and is provided hereinbelow with reference to the sequence listing part.

[12041] VGAM863 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM863 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM863 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12042] VGAM863 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM863 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM863 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM863 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM863 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12043] The complementary binding of VGAM863 RNA, herein designated VGAM RNA, to host target binding sites on VGAM863 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM863 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM863 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12044] It is appreciated that VGAM863 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM863 host target genes. The mRNA of each one of this plurality of VGAM863 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM863 RNA, herein designated VGAM RNA, and which when bound by VGAM863 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM863 host target proteins.

[12045] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM863 gene, herein designated VGAM GENE, on one or more VGAM863 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12046] It is yet further appreciated that a function of VGAM863 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM863 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Spe-

cific functions, and accordingly utilities, of VGAM863 correlate with, and may be deduced from, the identity of the host target genes which VGAM863 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12047] Nucleotide sequences of the VGAM863 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM863 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM863 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM863 are further described hereinbelow with reference to Table 1.

[12048] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM863 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12049] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 864 (VGAM864) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[12050] VGAM864 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM864 was detected is described hereinabove with reference to Figs. 2–8.

[12051] VGAM864 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM864 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12052] VGAM864 gene, herein designated VGAM GENE, encodes a VGAM864 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM864 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM864 precursor RNA is designated SEQ ID:23341, and is provided hereinbelow with reference to the sequence listing part.

[12053] VGAM864 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM864 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12054] An enzyme complex designated DICER COMPLEX, dices the VGAM864 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM864 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM864 RNA is designated SEQ ID:23342, and is provided hereinbelow with reference to the sequence listing part.

[12055] VGAM864 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM864 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM864 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12056] VGAM864 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM864 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM864 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM864 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM864 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12057] The complementary binding of VGAM864 RNA, herein designated VGAM RNA, to host target binding sites on VGAM864 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM864 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM864 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12058] It is appreciated that VGAM864 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM864 host target genes. The mRNA of each one of this plurality of VGAM864 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM864 RNA, herein designated VGAM RNA, and which when bound by VGAM864 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM864 host target proteins.

[12059] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM864 gene, herein designated VGAM GENE, on one or more VGAM864 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12060] It is yet further appreciated that a function of VGAM864 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM864 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM864 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM864 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12061] Nucleotide sequences of the VGAM864 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM864 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM864 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM864 are further described hereinbelow with reference to Table 1.

[12062] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM864 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12063] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 865 (VGAM865) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[12064] VGAM865 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM865 was detected is described hereinabove with reference to Figs. 2–8.

[12065] VGAM865 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM865 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12066] VGAM865 gene, herein designated VGAM GENE, encodes a VGAM865 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM865 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM865 precursor RNA is designated SEQ ID:23374, and is provided hereinbelow with reference to the sequence listing part.

[12067] VGAM865 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM865 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12068] An enzyme complex designated DICER COMPLEX, dices the VGAM865 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM865 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM865 RNA is designated SEQ ID:23375, and is provided hereinbelow with reference to the sequence listing part.

[12069] VGAM865 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM865 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM865 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12070] VGAM865 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM865 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM865 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM865 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM865 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12071] The complementary binding of VGAM865 RNA, herein designated VGAM RNA, to host target binding sites on VGAM865 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM865 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM865 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12072] It is appreciated that VGAM865 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM865 host target genes. The mRNA of each one of this plurality of VGAM865 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM865 RNA, herein designated VGAM RNA, and which when bound by VGAM865 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM865 host target proteins.

[12073] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM865 gene, herein designated VGAM GENE, on one or more VGAM865 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12074] It is yet further appreciated that a function of VGAM865 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM865 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM865 correlate with, and may be deduced from, the identity of the

host target genes which VGAM865 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12075] Nucleotide sequences of the VGAM865 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM865 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM865 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM865 are further described hereinbelow with reference to Table 1.

[12076] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM865 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12077] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 866 (VGAM866) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12078] VGAM866 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM866 was detected is described hereinabove with reference to Figs. 2–8.

[12079] VGAM866 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM866 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12080] VGAM866 gene, herein designated VGAM GENE, encodes a VGAM866 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM866 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM866 precursor RNA is designated SEQ ID:23386, and is provided hereinbelow with reference to the sequence listing part.

[12081] VGAM866 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM866 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12082] An enzyme complex designated DICER COMPLEX, dices the VGAM866 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM866 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM866 RNA is designated SEQ ID:23387, and is provided hereinbelow with reference to the sequence listing part.

[12083] VGAM866 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM866 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM866 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5



untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12084] VGAM866 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM866 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM866 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM866 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM866 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12085] The complementary binding of VGAM866 RNA, herein designated VGAM RNA, to host target binding sites on VGAM866 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM866 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM866 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12086] It is appreciated that VGAM866 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM866 host target genes. The mRNA of each one of this plurality of VGAM866 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM866 RNA, herein designated VGAM RNA, and which when bound by VGAM866 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM866 host target proteins.

[12087] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM866 gene, herein designated VGAM GENE, on one or more VGAM866 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12088] It is yet further appreciated that a function of VGAM866 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM866 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM866 correlate with, and may be deduced from, the identity of the host target genes which VGAM866 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[12089] Nucleotide sequences of the VGAM866 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM866 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM866 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM866 are further described hereinbelow with reference to Table 1.

[12090] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM866 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12091] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 867 (VGAM867) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12092] VGAM867 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM867 was detected is described hereinabove with reference to Figs. 2–8.

[12093] VGAM867 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM867 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12094] VGAM867 gene, herein designated VGAM GENE, encodes a VGAM867 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM867 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM867 precursor RNA is designated SEQ ID:23400, and is provided hereinbelow with reference to the sequence listing part.

[12095] VGAM867 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM867 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12096] An enzyme complex designated DICER COMPLEX, dices the VGAM867 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM867 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM867 RNA is designated SEQ ID:23401, and is provided hereinbelow with reference to the sequence listing part.

[12097] VGAM867 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM867 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM867 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12098] VGAM867 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM867 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM867 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM867 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM867 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[12099] The complementary binding of VGAM867 RNA, herein designated VGAM RNA, to host target binding sites on VGAM867 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM867 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM867 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12100] It is appreciated that VGAM867 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM867 host target genes. The mRNA of each one of this plurality of VGAM867 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM867 RNA, herein designated VGAM RNA, and which when bound by VGAM867 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM867 host target proteins.

[12101] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM867 gene, herein designated VGAM GENE, on one or more VGAM867 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12102] It is yet further appreciated that a function of VGAM867 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM867 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM867 correlate with, and may be deduced from, the identity of the host target genes which VGAM867 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[12103] Nucleotide sequences of the VGAM867 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM867 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM867 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM867 are further described hereinbelow with reference to Table 1.

[12104] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM867 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12105] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 868 (VGAM868) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12106] VGAM868 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM868 was detected is described hereinabove with reference to Figs. 2–8.

[12107] VGAM868 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM868 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12108] VGAM868 gene, herein designated VGAM GENE, encodes a VGAM868 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM868 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM868 precursor RNA is designated SEQ ID:23417, and is provided hereinbelow with reference to the sequence listing part.

[12109] VGAM868 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM868 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12110] An enzyme complex designated DICER COMPLEX, dices the VGAM868 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM868 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM868 RNA is designated SEQ ID:23418, and is provided hereinbelow with reference to the sequence listing part.

[12111] VGAM868 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM868 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM868 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[12112] VGAM868 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM868 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM868 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM868 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM868 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12113] The complementary binding of VGAM868 RNA, herein designated VGAM RNA, to host target binding sites on VGAM868 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM868 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM868 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12114] It is appreciated that VGAM868 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM868 host target genes. The mRNA of each one of this plurality of VGAM868 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM868 RNA, herein designated VGAM RNA, and which when bound by VGAM868 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM868 host target proteins.

[12115] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM868 gene, herein designated VGAM GENE, on one or

more VGAM868 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12116] It is yet further appreciated that a function of VGAM868 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM868 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM868 correlate with, and may be deduced from, the identity of the host target genes which VGAM868 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12117] Nucleotide sequences of the VGAM868 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM868 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM868 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM868 are further described hereinbelow with reference to Table 1.

[12118] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM868 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12119] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 869 (VGAM869) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12120] VGAM869 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM869 was detected is described



hereinabove with reference to Figs. 2–8.

[12121] VGAM869 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM869 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12122] VGAM869 gene, herein designated VGAM GENE, encodes a VGAM869 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM869 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM869 precursor RNA is designated SEQ ID:23426, and is provided hereinbelow with reference to the sequence listing part.

[12123] VGAM869 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM869 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12124] An enzyme complex designated DICER COMPLEX, dices the VGAM869 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM869 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM869 RNA is designated SEQ ID:23427, and is provided hereinbelow with reference to the sequence listing part.

[12125] VGAM869 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM869 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM869 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12126] VGAM869 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM869 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM869 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM869 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM869 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12127] The complementary binding of VGAM869 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM869 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM869 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM869 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12128] It is appreciated that VGAM869 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM869 host target genes. The mRNA of each one of this plurality of VGAM869 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM869 RNA, herein designated VGAM RNA, and which when bound by VGAM869 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM869 host target proteins.

[12129] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM869 gene, herein designated VGAM GENE, on one or more VGAM869 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12130] It is yet further appreciated that a function of VGAM869 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM869 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM869 correlate with, and may be deduced from, the identity of the host target genes which VGAM869 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12131] Nucleotide sequences of the VGAM869 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM869 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM869 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM869 are further described hereinbelow with reference to Table 1.

[12132] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM869 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12133] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 870 (VGAM870) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12134] VGAM870 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM870 was detected is described hereinabove with reference to Figs. 2-8.

[12135] VGAM870 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM870 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12136] VGAM870 gene, herein designated VGAM GENE, encodes a VGAM870 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM870 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM870 precursor RNA is designated SEQ ID:23443, and is provided hereinbelow with reference to the sequence listing part.

[12137] VGAM870 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM870 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[12138] An enzyme complex designated DICER COMPLEX, dices the VGAM870 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM870 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM870 RNA is designated SEQ ID:23444, and is provided hereinbelow with reference to the sequence listing part.

[12139] VGAM870 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM870 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM870 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12140] VGAM870 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM870 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM870 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM870 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM870 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12141] The complementary binding of VGAM870 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM870 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM870 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM870 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12142] It is appreciated that VGAM870 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM870 host target genes. The mRNA of each one of this plurality of VGAM870 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM870 RNA, herein designated VGAM RNA, and which when bound by VGAM870 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM870 host target proteins.

[12143] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM870 gene, herein designated VGAM GENE, on one or more VGAM870 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12144] It is yet further appreciated that a function of VGAM870 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM870 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM870 correlate with, and may be deduced from, the identity of the host target genes which VGAM870 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12145] Nucleotide sequences of the VGAM870 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM870 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM870 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM870 are further described hereinbelow with reference to Table 1.

[12146] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM870 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12147] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 871 (VGAM871) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12148] VGAM871 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM871 was detected is described hereinabove with reference to Figs. 2-8.

[12149] VGAM871 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Melanoplus sanguinipes* entomopoxvirus. VGAM871 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12150] VGAM871 gene, herein designated VGAM GENE, encodes a VGAM871 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM871 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM871 precursor RNA is designated SEQ ID:23450, and is provided hereinbelow with reference to the sequence listing part.

[12151] VGAM871 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM871 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12152] An enzyme complex designated DICER COMPLEX, dices the VGAM871 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM871 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM871 RNA is designated SEQ ID:23451, and is provided hereinbelow with reference to the sequence listing part.

[12153] VGAM871 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM871 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM871 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12154] VGAM871 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM871 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM871 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM871 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM871 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12155] The complementary binding of VGAM871 RNA, herein designated VGAM RNA, to host target binding sites on VGAM871 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM871 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM871 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12156] It is appreciated that VGAM871 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM871 host target genes. The mRNA of each one of this plurality of VGAM871 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM871 RNA, herein designated VGAM RNA, and which when bound by VGAM871 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM871 host target proteins.

[12157] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM871 gene, herein designated VGAM GENE, on one or more VGAM871 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12158] It is yet further appreciated that a function of VGAM871 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM871 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM871 correlate with, and may be deduced from, the identity of the host target genes which VGAM871 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12159] Nucleotide sequences of the VGAM871 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM871 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM871 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM871 are further described hereinbelow with reference to Table 1.

[12160] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM871 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12161] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 872 (VGAM872) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12162] VGAM872 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM872 was detected is described hereinabove with reference to Figs. 2-8.

[12163] VGAM872 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Melanoplus sanguinipes*

entomopoxvirus. VGAM872 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12164] VGAM872 gene, herein designated VGAM GENE, encodes a VGAM872 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM872 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM872 precursor RNA is designated SEQ ID:23463, and is provided hereinbelow with reference to the sequence listing part.

[12165] VGAM872 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM872 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12166] An enzyme complex designated DICER COMPLEX, dices

the VGAM872 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM872 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM872 RNA is designated SEQ ID:23464, and is provided hereinbelow with reference to the sequence listing part.

[12167] VGAM872 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM872 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM872 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12168] VGAM872 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM872 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM872 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM872 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM872 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12169] The complementary binding of VGAM872 RNA, herein designated VGAM RNA, to host target binding sites on VGAM872 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM872 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM872 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12170] It is appreciated that VGAM872 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM872 host target genes. The mRNA of each one of this plurality of VGAM872 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM872 RNA, herein designated VGAM RNA, and which when bound by VGAM872 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM872 host target proteins.

[12171] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM872 gene, herein designated VGAM GENE, on one or more VGAM872 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12172] It is yet further appreciated that a function of VGAM872 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM872 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM872 correlate with, and may be deduced from, the identity of the host target genes which VGAM872 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12173] Nucleotide sequences of the VGAM872 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM872 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM872 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM872 are further described hereinbelow with reference to Table 1.

[12174] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM872 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12175] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 873 (VGAM873) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12176] VGAM873 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM873 was detected is described hereinabove with reference to Figs. 2-8.

[12177] VGAM873 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM873 host target gene, herein des-



ignated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12178] VGAM873 gene, herein designated VGAM GENE, encodes a VGAM873 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM873 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM873 precursor RNA is designated SEQ ID:23469, and is provided hereinbelow with reference to the sequence listing part.

[12179] VGAM873 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM873 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12180] An enzyme complex designated DICER COMPLEX, dices the VGAM873 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM873 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM873 RNA is designated SEQ ID:23470, and is provided hereinbelow with reference to the sequence listing part.

[12181] VGAM873 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM873 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM873 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12182] VGAM873 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM873 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM873 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM873 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM873 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12183] The complementary binding of VGAM873 RNA, herein designated VGAM RNA, to host target binding sites on VGAM873 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM873 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM873 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12184] It is appreciated that VGAM873 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM873 host target genes. The mRNA of each one of this plurality of VGAM873 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM873 RNA, herein designated VGAM RNA, and which when bound by VGAM873 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM873 host target proteins.

[12185] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM873 gene, herein designated VGAM GENE, on one or more VGAM873 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12186] It is yet further appreciated that a function of VGAM873 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM873 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM873 correlate with, and may be deduced from, the identity of the host target genes which VGAM873 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12187] Nucleotide sequences of the VGAM873 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM873 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM873 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM873 are further described hereinbelow with reference to Table 1.

[12188] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM873 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12189] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 874 (VGAM874) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12190] VGAM874 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM874 was detected is described hereinabove with reference to Figs. 2-8.

[12191] VGAM874 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM874 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[12192] VGAM874 gene, herein designated VGAM GENE, encodes a VGAM874 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM874 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM874 precursor RNA is designated SEQ ID:23477, and is provided hereinbelow with reference to the sequence listing part.

[12193] VGAM874 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM874 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12194] An enzyme complex designated DICER COMPLEX, dices the VGAM874 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM874 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM874 RNA is designated SEQ ID:23478, and is provided hereinbelow with reference to the sequence listing part.

[12195] VGAM874 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM874 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM874 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12196] VGAM874 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM874 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM874 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM874 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM874 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12197] The complementary binding of VGAM874 RNA, herein designated VGAM RNA, to host target binding sites on VGAM874 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM874 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM874 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12198] It is appreciated that VGAM874 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM874 host target genes. The mRNA of each one of this plurality of VGAM874 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM874 RNA, herein designated VGAM RNA, and which when bound by VGAM874 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM874 host target proteins.

[12199] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM874 gene, herein designated VGAM GENE, on one or more VGAM874 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12200] It is yet further appreciated that a function of VGAM874 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM874 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM874 correlate with, and may be deduced from, the identity of the host target genes which VGAM874 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12201] Nucleotide sequences of the VGAM874 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM874 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM874 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM874 are further de-

scribed hereinbelow with reference to Table 1.

[12202] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM874 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12203] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 875 (VGAM875) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12204] VGAM875 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM875 was detected is described hereinabove with reference to Figs. 2-8.

[12205] VGAM875 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM875 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12206] VGAM875 gene, herein designated VGAM GENE, encodes a VGAM875 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM875 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM875 precursor RNA is designated SEQ ID:23527, and is provided hereinbelow with reference to the sequence listing part.

[12207] VGAM875 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM875 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12208] An enzyme complex designated DICER COMPLEX, dices the VGAM875 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM875 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM875 RNA is designated SEQ ID:23528, and is provided hereinbelow with reference to the sequence listing part.

[12209] VGAM875 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM875 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM875 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12210] VGAM875 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM875 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM875 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM875 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM875 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12211] The complementary binding of VGAM875 RNA, herein designated VGAM RNA, to host target binding sites on VGAM875 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM875 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM875 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12212] It is appreciated that VGAM875 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM875 host target genes. The mRNA of each one of this plurality of VGAM875 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM875 RNA, herein designated VGAM RNA, and which when bound by VGAM875 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM875 host target proteins.

[12213] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM875 gene, herein designated VGAM GENE, on one or more VGAM875 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12214] It is yet further appreciated that a function of VGAM875 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM875 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM875 correlate with, and may be deduced from, the identity of the host target genes which VGAM875 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12215] Nucleotide sequences of the VGAM875 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM875 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM875 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM875 are further described hereinbelow with reference to Table 1.

[12216] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM875 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12217] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 876 (VGAM876) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12218] VGAM876 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM876 was detected is described hereinabove with reference to Figs. 2-8.

[12219] VGAM876 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM876 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12220] VGAM876 gene, herein designated VGAM GENE, encodes a

VGAM876 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM876 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM876 precursor RNA is designated SEQ ID:23541, and is provided hereinbelow with reference to the sequence listing part.

[12221] VGAM876 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM876 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12222] An enzyme complex designated DICER COMPLEX, dices the VGAM876 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM876 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM876 RNA is designated SEQ ID:23542, and is provided hereinbelow with reference to the sequence listing part.

[12223] VGAM876 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM876 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM876 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12224] VGAM876 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM876 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM876 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM876 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM876 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12225] The complementary binding of VGAM876 RNA, herein designated VGAM RNA, to host target binding sites on VGAM876 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM876 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM876 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[12226] It is appreciated that VGAM876 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM876 host target genes. The mRNA of each one of this plurality of VGAM876 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM876 RNA, herein designated VGAM RNA, and which when bound by VGAM876 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM876 host target proteins.

[12227] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM876 gene, herein designated VGAM GENE, on one or more VGAM876 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12228] It is yet further appreciated that a function of VGAM876 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM876 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM876 correlate with, and may be deduced from, the identity of the host target genes which VGAM876 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12229] Nucleotide sequences of the VGAM876 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM876 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM876 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM876 are further described hereinbelow with reference to Table 1.

[12230] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM876 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12231] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 877 (VGAM877) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12232] VGAM877 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM877 was detected is described hereinabove with reference to Figs. 2-8.

[12233] VGAM877 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 40. VGAM877 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12234] VGAM877 gene, herein designated VGAM GENE, encodes a VGAM877 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM877 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM877 precursor RNA is designated SEQ ID:23559, and is provided hereinbelow with reference to the sequence listing part.

[12235] VGAM877 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM877 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12236] An enzyme complex designated DICER COMPLEX, dices the VGAM877 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM877 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM877 RNA is designated SEQ ID:23560, and is provided hereinbelow with reference to the sequence listing part.

[12237] VGAM877 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM877 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM877 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12238] VGAM877 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM877 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM877 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM877 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM877 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12239] The complementary binding of VGAM877 RNA, herein designated VGAM RNA, to host target binding sites on VGAM877 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM877 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM877 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12240] It is appreciated that VGAM877 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM877 host target genes. The mRNA of each one of this plurality of VGAM877 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM877 RNA, herein designated VGAM RNA, and which when bound by VGAM877 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM877 host target proteins.

[12241] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM877 gene, herein designated VGAM GENE, on one or more VGAM877 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12242] It is yet further appreciated that a function of VGAM877 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM877 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 40. Specific functions, and accordingly utilities, of VGAM877 correlate with, and may be deduced from, the identity of the host target genes which VGAM877 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12243] Nucleotide sequences of the VGAM877 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM877 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM877 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM877 are further described hereinbelow with reference to Table 1.

[12244] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM877 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12245] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 878 (VGAM878) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12246] VGAM878 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM878 was detected is described hereinabove with reference to Figs. 2-8.

[12247] VGAM878 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 40. VGAM878 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12248] VGAM878 gene, herein designated VGAM GENE, encodes a VGAM878 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM878 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM878 precursor RNA is designated SEQ ID:23571, and is provided hereinbelow with reference to the sequence listing part.

[12249] VGAM878 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM878 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[12250] An enzyme complex designated DICER COMPLEX, dices the VGAM878 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM878 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM878 RNA is designated SEQ ID:23572, and is provided hereinbelow with reference to the sequence listing part.

[12251] VGAM878 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM878 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM878 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12252] VGAM878 RNA, herein designated VGAM RNA, binds com-



plementarily to one or more host target binding sites located in untranslated regions of VGAM878 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM878 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM878 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM878 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12253] The complementary binding of VGAM878 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM878 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM878 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM878 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12254] It is appreciated that VGAM878 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM878 host target genes. The mRNA of each one of this plurality of VGAM878 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM878 RNA, herein designated VGAM RNA, and which when bound by VGAM878 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM878 host target proteins.

[12255] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM878 gene, herein designated VGAM GENE, on one or more VGAM878 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12256] It is yet further appreciated that a function of VGAM878 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM878 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 40. Specific functions, and accordingly utilities, of VGAM878 correlate with, and may be deduced from, the identity of the host target genes which VGAM878 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12257] Nucleotide sequences of the VGAM878 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM878 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM878 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM878 are further described hereinbelow with reference to Table 1.

[12258] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM878 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12259] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 879 (VGAM879) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12260] VGAM879 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM879 was detected is described hereinabove with reference to Figs. 2-8.

[12261] VGAM879 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Paramecium bursaria* Chlorella virus 1. VGAM879 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12262] VGAM879 gene, herein designated VGAM GENE, encodes a VGAM879 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM879 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM879 precursor RNA is designated SEQ ID:23580, and is provided hereinbelow with reference to the sequence listing part.

[12263] VGAM879 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM879 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12264] An enzyme complex designated DICER COMPLEX, dices the VGAM879 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM879 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM879 RNA is designated SEQ ID:23581, and is provided hereinbelow with reference to the sequence listing part.

[12265] VGAM879 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM879 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM879 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12266] VGAM879 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM879 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM879 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM879 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM879 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12267] The complementary binding of VGAM879 RNA, herein designated VGAM RNA, to host target binding sites on VGAM879 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM879 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM879 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12268] It is appreciated that VGAM879 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM879 host target genes. The mRNA of each one of this plurality of VGAM879 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM879 RNA, herein designated VGAM RNA, and which when bound by VGAM879 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM879 host target proteins.

[12269] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM879 gene, herein designated VGAM GENE, on one or more VGAM879 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12270] It is yet further appreciated that a function of VGAM879 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM879 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM879 correlate with, and may be deduced from, the identity of the host target genes which VGAM879 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12271] Nucleotide sequences of the VGAM879 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM879 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM879 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM879 are further described hereinbelow with reference to Table 1.

[12272] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM879 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12273] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 880 (VGAM880) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12274] VGAM880 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM880 was detected is described hereinabove with reference to Figs. 2-8.

[12275] VGAM880 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM880 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12276] VGAM880 gene, herein designated VGAM GENE, encodes a VGAM880 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM880 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM880 precursor RNA is designated SEQ ID:23601, and is provided hereinbelow with reference to the sequence listing part.

[12277] VGAM880 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM880 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12278] An enzyme complex designated DICER COMPLEX, dices

the VGAM880 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM880 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM880 RNA is designated SEQ ID:23602, and is provided hereinbelow with reference to the sequence listing part.

[12279] VGAM880 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM880 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM880 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12280] VGAM880 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM880 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM880 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM880 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM880 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12281] The complementary binding of VGAM880 RNA, herein designated VGAM RNA, to host target binding sites on VGAM880 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM880 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM880 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12282] It is appreciated that VGAM880 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM880 host target genes. The mRNA of each one of this plurality of VGAM880 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM880 RNA, herein designated VGAM RNA, and which when bound by VGAM880 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM880 host target proteins.

[12283] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM880 gene, herein designated VGAM GENE, on one or more VGAM880 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12284] It is yet further appreciated that a function of VGAM880 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM880 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM880 correlate with, and may be deduced from, the identity of the host target genes which VGAM880 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12285] Nucleotide sequences of the VGAM880 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM880 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM880 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM880 are further described hereinbelow with reference to Table 1.

[12286] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM880 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12287] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 881 (VGAM881) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12288] VGAM881 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM881 was detected is described hereinabove with reference to Figs. 2-8.

[12289] VGAM881 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM881 host target gene, herein des-



ignated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12290] VGAM881 gene, herein designated VGAM GENE, encodes a VGAM881 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM881 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM881 precursor RNA is designated SEQ ID:23617, and is provided hereinbelow with reference to the sequence listing part.

[12291] VGAM881 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM881 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12292] An enzyme complex designated DICER COMPLEX, dices the VGAM881 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM881 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM881 RNA is designated SEQ ID:23618, and is provided hereinbelow with reference to the sequence listing part.

[12293] VGAM881 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM881 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM881 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12294] VGAM881 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM881 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM881 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM881 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM881 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12295] The complementary binding of VGAM881 RNA, herein designated VGAM RNA, to host target binding sites on VGAM881 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM881 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM881 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12296] It is appreciated that VGAM881 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM881 host target genes. The mRNA of each one of this plurality of VGAM881 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM881 RNA, herein designated VGAM RNA, and which when bound by VGAM881 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM881 host target proteins.

[12297] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM881 gene, herein designated VGAM GENE, on one or more VGAM881 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12298] It is yet further appreciated that a function of VGAM881 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM881 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM881 correlate with, and may be deduced from, the identity of the host target genes which VGAM881 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12299] Nucleotide sequences of the VGAM881 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM881 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM881 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM881 are further described hereinbelow with reference to Table 1.

[12300] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM881 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12301] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 882 (VGAM882) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12302] VGAM882 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM882 was detected is described hereinabove with reference to Figs. 2-8.

[12303] VGAM882 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM882 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[12304] VGAM882 gene, herein designated VGAM GENE, encodes a VGAM882 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM882 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM882 precursor RNA is designated SEQ ID:23620, and is provided hereinbelow with reference to the sequence listing part.

[12305] VGAM882 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM882 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12306] An enzyme complex designated DICER COMPLEX, dices the VGAM882 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM882 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM882 RNA is designated SEQ ID:23621, and is provided hereinbelow with reference to the sequence listing part.

[12307] VGAM882 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM882 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM882 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12308] VGAM882 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM882 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM882 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM882 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM882 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12309] The complementary binding of VGAM882 RNA, herein designated VGAM RNA, to host target binding sites on VGAM882 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM882 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM882 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12310] It is appreciated that VGAM882 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM882 host target genes. The mRNA of each one of this plurality of VGAM882 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM882 RNA, herein designated VGAM RNA, and which when bound by VGAM882 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM882 host target proteins.

[12311] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM882 gene, herein designated VGAM GENE, on one or more VGAM882 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12312] It is yet further appreciated that a function of VGAM882 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM882 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM882 correlate with, and may be deduced from, the identity of the host target genes which VGAM882 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12313] Nucleotide sequences of the VGAM882 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM882 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM882 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM882 are further de-

scribed hereinbelow with reference to Table 1.

[12314] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM882 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12315] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 883 (VGAM883) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12316] VGAM883 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM883 was detected is described hereinabove with reference to Figs. 2-8.

[12317] VGAM883 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus. VGAM883 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12318] VGAM883 gene, herein designated VGAM GENE, encodes a VGAM883 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM883 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM883 precursor RNA is designated SEQ ID:23627, and is provided hereinbelow with reference to the sequence listing part.

[12319] VGAM883 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM883 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12320] An enzyme complex designated DICER COMPLEX, dices the VGAM883 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM883 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM883 RNA is designated SEQ ID:23628, and is provided hereinbelow with reference to the sequence listing part.

[12321] VGAM883 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM883 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM883 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12322] VGAM883 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM883 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM883 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM883 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM883 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12323] The complementary binding of VGAM883 RNA, herein designated VGAM RNA, to host target binding sites on VGAM883 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM883 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM883 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12324] It is appreciated that VGAM883 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM883 host target genes. The mRNA of each one of this plurality of VGAM883 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM883 RNA, herein designated VGAM RNA, and which when bound by VGAM883 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM883 host target proteins.

[12325] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM883 gene, herein designated VGAM GENE, on one or more VGAM883 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12326] It is yet further appreciated that a function of VGAM883 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM883 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM883 correlate with, and may be deduced from, the identity of the host target genes which VGAM883 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12327] Nucleotide sequences of the VGAM883 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM883 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM883 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM883 are further described hereinbelow with reference to Table 1.

[12328] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM883 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12329] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 884 (VGAM884) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12330] VGAM884 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM884 was detected is described hereinabove with reference to Figs. 2-8.

[12331] VGAM884 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Marburg virus.

VGAM884 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12332] VGAM884 gene, herein designated VGAM GENE, encodes a

VGAM884 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM884 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM884 precursor RNA is designated SEQ ID:23637, and is provided hereinbelow with reference to the sequence listing part.

[12333] VGAM884 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM884 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12334] An enzyme complex designated DICER COMPLEX, dices the VGAM884 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM884 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM884 RNA is designated SEQ ID:23638, and is provided hereinbelow with reference to the sequence listing part.

[12335] VGAM884 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM884 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM884 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12336] VGAM884 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM884 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM884 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM884 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM884 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12337] The complementary binding of VGAM884 RNA, herein designated VGAM RNA, to host target binding sites on VGAM884 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM884 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM884 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[12338] It is appreciated that VGAM884 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM884 host target genes. The mRNA of each one of this plurality of VGAM884 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM884 RNA, herein designated VGAM RNA, and which when bound by VGAM884 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM884 host target proteins.

[12339] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM884 gene, herein designated VGAM GENE, on one or more VGAM884 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12340] It is yet further appreciated that a function of VGAM884 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM884 include diagnosis, prevention and treatment of viral infection by Marburg virus. Specific functions, and accordingly utilities, of VGAM884 correlate with, and may be deduced from, the identity of the host target genes which VGAM884 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12341] Nucleotide sequences of the VGAM884 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM884 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM884 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM884 are further described hereinbelow with reference to Table 1.

[12342] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM884 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12343] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 885 (VGAM885) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12344] VGAM885 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM885 was detected is described hereinabove with reference to Figs. 2-8.

[12345] VGAM885 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM885 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12346] VGAM885 gene, herein designated VGAM GENE, encodes a VGAM885 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM885 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM885 precursor RNA is designated SEQ ID:23653, and is provided hereinbelow with reference to the sequence listing part.

[12347] VGAM885 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM885 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12348] An enzyme complex designated DICER COMPLEX, dices the VGAM885 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM885 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM885 RNA is designated SEQ ID:23654, and is provided hereinbelow with reference to the sequence listing part.

[12349] VGAM885 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM885 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM885 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12350] VGAM885 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM885 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM885 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM885 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM885 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12351] The complementary binding of VGAM885 RNA, herein designated VGAM RNA, to host target binding sites on VGAM885 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM885 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM885 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12352] It is appreciated that VGAM885 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM885 host target genes. The mRNA of each one of this plurality of VGAM885 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM885 RNA, herein designated VGAM RNA, and which when bound by VGAM885 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM885 host target proteins.

[12353] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM885 gene, herein designated VGAM GENE, on one or more VGAM885 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12354] It is yet further appreciated that a function of VGAM885 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM885 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM885 correlate with, and may be deduced from, the identity of the host target genes which VGAM885 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12355] Nucleotide sequences of the VGAM885 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM885 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM885 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM885 are further described hereinbelow with reference to Table 1.

[12356] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM885 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12357] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 886 (VGAM886) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12358] VGAM886 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM886 was detected is described hereinabove with reference to Figs. 2–8.

[12359] VGAM886 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM886 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12360] VGAM886 gene, herein designated VGAM GENE, encodes a VGAM886 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM886 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM886 precursor RNA is designated SEQ ID:23657, and is provided hereinbelow with reference to the sequence listing part.

[12361] VGAM886 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM886 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12362] An enzyme complex designated DICER COMPLEX, dices the VGAM886 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM886 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM886 RNA is designated SEQ ID:23658, and is provided hereinbelow with reference to the sequence listing part.

[12363] VGAM886 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM886 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM886 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12364] VGAM886 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM886 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM886 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM886 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM886 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12365] The complementary binding of VGAM886 RNA, herein designated VGAM RNA, to host target binding sites on VGAM886 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM886 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM886 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12366] It is appreciated that VGAM886 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM886 host target genes. The mRNA of each one of this plurality of VGAM886 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM886 RNA, herein designated VGAM RNA, and which when bound by VGAM886 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM886 host target proteins.

[12367] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM886 gene, herein designated VGAM GENE, on one or more VGAM886 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12368] It is yet further appreciated that a function of VGAM886 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM886 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM886 correlate with, and may be deduced from, the identity of the host target genes which VGAM886 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12369] Nucleotide sequences of the VGAM886 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM886 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM886 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM886 are further described hereinbelow with reference to Table 1.

[12370] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM886 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12371] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 887 (VGAM887) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12372] VGAM887 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM887 was detected is described hereinabove with reference to Figs. 2–8.

[12373] VGAM887 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM887 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12374] VGAM887 gene, herein designated VGAM GENE, encodes a VGAM887 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM887 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM887 precursor RNA is designated SEQ ID:23666, and is provided hereinbelow with reference to the sequence listing part.

[12375] VGAM887 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM887 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12376] An enzyme complex designated DICER COMPLEX, dices the VGAM887 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM887 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM887 RNA is designated SEQ ID:23667, and is provided hereinbelow with reference to the sequence listing part.

[12377] VGAM887 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM887 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM887 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12378] VGAM887 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM887 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM887 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM887 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM887 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12379] The complementary binding of VGAM887 RNA, herein designated VGAM RNA, to host target binding sites on VGAM887 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM887 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM887 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12380] It is appreciated that VGAM887 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM887 host target genes. The mRNA of each one of this plurality of VGAM887 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM887 RNA, herein designated VGAM RNA, and which when bound by VGAM887 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM887 host target proteins.

[12381] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM887 gene, herein designated VGAM GENE, on one or more VGAM887 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [12382] It is yet further appreciated that a function of VGAM887 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM887 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM887 correlate with, and may be deduced from, the identity of the host target genes which VGAM887 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [12383] Nucleotide sequences of the VGAM887 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM887 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM887 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM887 are further described hereinbelow with reference to Table 1.
- [12384] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM887 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12385] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 888 (VGAM888) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12386] VGAM888 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM888 was detected is described hereinabove with reference to Figs. 2–8.

[12387] VGAM888 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 3. VGAM888 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12388] VGAM888 gene, herein designated VGAM GENE, encodes a VGAM888 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM888 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM888 precursor RNA is designated SEQ ID:23676, and is provided hereinbelow with reference to the sequence listing part.

[12389] VGAM888 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM888 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12390] An enzyme complex designated DICER COMPLEX, dices the VGAM888 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM888 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM888 RNA is designated SEQ ID:23677, and is provided hereinbelow with reference to the sequence listing part.

[12391] VGAM888 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM888 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM888 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12392] VGAM888 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM888 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM888 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM888 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM888 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12393] The complementary binding of VGAM888 RNA, herein designated VGAM RNA, to host target binding sites on VGAM888 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM888 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM888 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12394] It is appreciated that VGAM888 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM888 host target genes. The mRNA of

each one of this plurality of VGAM888 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM888 RNA, herein designated VGAM RNA, and which when bound by VGAM888 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM888 host target proteins.

[12395] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM888 gene, herein designated VGAM GENE, on one or more VGAM888 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[12396] It is yet further appreciated that a function of VGAM888 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM888 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 3. Specific functions, and accordingly utilities, of VGAM888 correlate with, and may be deduced from, the identity of the host target genes which VGAM888 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12397] Nucleotide sequences of the VGAM888 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM888 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM888 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM888 are further described hereinbelow with reference to Table 1.

[12398] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM888 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[12399] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 889 (VGAM889) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12400] VGAM889 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM889 was detected is described hereinabove with reference to Figs. 2–8.

[12401] VGAM889 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus D. VGAM889 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12402] VGAM889 gene, herein designated VGAM GENE, encodes a VGAM889 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM889 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar



to the nucleotide sequence of VGAM889 precursor RNA is designated SEQ ID:23679, and is provided hereinbelow with reference to the sequence listing part.

[12403] VGAM889 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM889 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12404] An enzyme complex designated DICER COMPLEX, dices the VGAM889 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM889 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM889 RNA is designated SEQ ID:23680, and

is provided hereinbelow with reference to the sequence listing part.

[12405] VGAM889 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM889 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM889 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12406] VGAM889 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM889 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM889 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM889 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM889 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12407] The complementary binding of VGAM889 RNA, herein designated VGAM RNA, to host target binding sites on VGAM889 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM889 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM889 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12408] It is appreciated that VGAM889 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM889 host target genes. The mRNA of each one of this plurality of VGAM889 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM889 RNA, herein designated VGAM RNA, and which when bound by VGAM889 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM889 host target proteins.

[12409] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM889 gene, herein designated VGAM GENE, on one or more VGAM889 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12410] It is yet further appreciated that a function of VGAM889 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM889 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus D. Specific functions, and accordingly utilities, of VGAM889 correlate with, and may be deduced from, the identity of the host target genes which VGAM889 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12411] Nucleotide sequences of the VGAM889 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM889 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM889 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM889 are further described hereinbelow with reference to Table 1.

[12412] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM889 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12413] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 890 (VGAM890) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12414] VGAM890 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM890 was detected is described hereinabove with reference to Figs. 2–8.

[12415] VGAM890 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus D. VGAM890 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12416] VGAM890 gene, herein designated VGAM GENE, encodes a VGAM890 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM890 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM890 precursor RNA is

designated SEQ ID:23682, and is provided hereinbelow with reference to the sequence listing part.

[12417] VGAM890 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM890 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12418] An enzyme complex designated DICER COMPLEX, dices the VGAM890 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM890 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM890 RNA is designated SEQ ID:23683, and is provided hereinbelow with reference to the sequence

listing part.

[12419] VGAM890 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM890 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM890 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12420] VGAM890 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM890 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM890 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM890 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM890 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12421] The complementary binding of VGAM890 RNA, herein designated VGAM RNA, to host target binding sites on VGAM890 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM890 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM890 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12422] It is appreciated that VGAM890 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM890 host target genes. The mRNA of each one of this plurality of VGAM890 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM890 RNA, herein designated VGAM RNA, and which when bound by VGAM890 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM890 host target proteins.

[12423] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM890 gene, herein designated VGAM GENE, on one or more VGAM890 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12424] It is yet further appreciated that a function of VGAM890 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM890 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus D. Specific functions, and accordingly utilities, of VGAM890 correlate with, and may be deduced from, the identity of the host target genes which VGAM890 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[12425] Nucleotide sequences of the VGAM890 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM890 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM890 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM890 are further described hereinbelow with reference to Table 1.

[12426] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM890 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12427] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 891 (VGAM891) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12428] VGAM891 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM891 was detected is described hereinabove with reference to Figs. 2–8.

[12429] VGAM891 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM891 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12430] VGAM891 gene, herein designated VGAM GENE, encodes a VGAM891 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM891 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM891 precursor RNA is designated SEQ ID:23690, and is provided hereinbelow

with reference to the sequence listing part.

[12431] VGAM891 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM891 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12432] An enzyme complex designated DICER COMPLEX, dices the VGAM891 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM891 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM891 RNA is designated SEQ ID:23691, and is provided hereinbelow with reference to the sequence listing part.

[12433] VGAM891 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM891 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM891 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12434] VGAM891 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM891 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM891 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM891 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM891 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12435] The complementary binding of VGAM891 RNA, herein designated VGAM RNA, to host target binding sites on VGAM891 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM891 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM891 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12436] It is appreciated that VGAM891 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM891 host target genes. The mRNA of each one of this plurality of VGAM891 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM891 RNA, herein designated VGAM RNA, and which when bound by VGAM891 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM891 host target proteins.

[12437] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM891 gene, herein designated VGAM GENE, on one or more VGAM891 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12438] It is yet further appreciated that a function of VGAM891 is inhibition of expression of host target genes, as part of a



novel viral mechanism of attacking a host. Accordingly, utilities of VGAM891 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM891 correlate with, and may be deduced from, the identity of the host target genes which VGAM891 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12439] Nucleotide sequences of the VGAM891 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM891 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM891 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM891 are further described hereinbelow with reference to Table 1.

[12440] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM891 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12441] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 892 (VGAM892) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12442] VGAM892 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM892 was detected is described hereinabove with reference to Figs. 2–8.

[12443] VGAM892 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM892 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12444] VGAM892 gene, herein designated VGAM GENE, encodes a VGAM892 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM892 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM892 precursor RNA is designated SEQ ID:23696, and is provided hereinbelow with reference to the sequence listing part.

[12445] VGAM892 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM892 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12446] An enzyme complex designated DICER COMPLEX, dices the VGAM892 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM892 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM892 RNA is designated SEQ ID:23697, and is provided hereinbelow with reference to the sequence listing part.

[12447] VGAM892 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM892 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM892 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12448] VGAM892 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM892 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM892 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM892 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM892 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12449] The complementary binding of VGAM892 RNA, herein designated VGAM RNA, to host target binding sites on VGAM892 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM892 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM892 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12450] It is appreciated that VGAM892 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM892 host target genes. The mRNA of each one of this plurality of VGAM892 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM892 RNA, herein designated VGAM

RNA, and which when bound by VGAM892 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM892 host target proteins.

[12451] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM892 gene, herein designated VGAM GENE, on one or more VGAM892 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12452] It is yet further appreciated that a function of VGAM892 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM892 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM892 correlate with, and may be deduced from, the identity of the host target genes which VGAM892 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12453] Nucleotide sequences of the VGAM892 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM892 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM892 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM892 are further described hereinbelow with reference to Table 1.

[12454] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM892 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12455] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 893 (VGAM893) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12456] VGAM893 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM893 was detected is described hereinabove with reference to Figs. 2–8.

[12457] VGAM893 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM893 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12458] VGAM893 gene, herein designated VGAM GENE, encodes a VGAM893 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM893 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM893 precursor RNA is designated SEQ ID:23705, and is provided hereinbelow with reference to the sequence listing part.

[12459] VGAM893 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM893 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12460] An enzyme complex designated DICER COMPLEX, dices the VGAM893 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM893 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM893 RNA is designated SEQ ID:23706, and is provided hereinbelow with reference to the sequence listing part.

[12461] VGAM893 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM893 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM893 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12462] VGAM893 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM893 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM893 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM893 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM893 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12463] The complementary binding of VGAM893 RNA, herein designated VGAM RNA, to host target binding sites on VGAM893 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM893 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM893 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12464] It is appreciated that VGAM893 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM893 host target genes. The mRNA of each one of this plurality of VGAM893 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM893 RNA, herein designated VGAM RNA, and which when bound by VGAM893 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM893 host target proteins.

[12465] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM893 gene, herein designated VGAM GENE, on one or more VGAM893 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12466] It is yet further appreciated that a function of VGAM893 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM893 include diagnosis, prevention and

treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM893 correlate with, and may be deduced from, the identity of the host target genes which VGAM893 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12467] Nucleotide sequences of the VGAM893 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM893 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM893 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM893 are further described hereinbelow with reference to Table 1.

[12468] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM893 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12469] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 894 (VGAM894) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12470] VGAM894 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM894 was detected is described hereinabove with reference to Figs. 2–8.

[12471] VGAM894 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM894 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12472] VGAM894 gene, herein designated VGAM GENE, encodes a VGAM894 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM894 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM894 precursor RNA is designated SEQ ID:23713, and is provided hereinbelow with reference to the sequence listing part.

[12473] VGAM894 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM894 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12474] An enzyme complex designated DICER COMPLEX, dices the VGAM894 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM894 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM894 RNA is designated SEQ ID:23714, and is provided hereinbelow with reference to the sequence listing part.

[12475] VGAM894 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM894 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM894 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12476] VGAM894 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM894 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM894 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM894 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM894 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12477] The complementary binding of VGAM894 RNA, herein designated VGAM RNA, to host target binding sites on VGAM894 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM894 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM894 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12478] It is appreciated that VGAM894 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM894 host target genes. The mRNA of each one of this plurality of VGAM894 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM894 RNA, herein designated VGAM RNA, and which when bound by VGAM894 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM894 host target proteins.

[12479] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM894 gene, herein designated VGAM GENE, on one or more VGAM894 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12480] It is yet further appreciated that a function of VGAM894 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM894 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus

7. Specific functions, and accordingly utilities, of VGAM894 correlate with, and may be deduced from, the identity of the host target genes which VGAM894 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12481] Nucleotide sequences of the VGAM894 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM894 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM894 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM894 are further described hereinbelow with reference to Table 1.

[12482] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM894 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12483] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 895 (VGAM895) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[12484] VGAM895 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM895 was detected is described hereinabove with reference to Figs. 2–8.

[12485] VGAM895 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM895 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12486] VGAM895 gene, herein designated VGAM GENE, encodes a VGAM895 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM895 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM895 precursor RNA is designated SEQ ID:23746, and is provided hereinbelow with reference to the sequence listing part.

[12487] VGAM895 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM895 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12488] An enzyme complex designated DICER COMPLEX, dices the VGAM895 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM895 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM895 RNA is designated SEQ ID:23747, and is provided hereinbelow with reference to the sequence listing part.

[12489] VGAM895 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM895 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM895 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12490] VGAM895 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM895 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM895 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM895 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM895 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12491] The complementary binding of VGAM895 RNA, herein designated VGAM RNA, to host target binding sites on VGAM895 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM895 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM895 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12492] It is appreciated that VGAM895 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM895 host target genes. The mRNA of each one of this plurality of VGAM895 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM895 RNA, herein designated VGAM RNA, and which when bound by VGAM895 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM895 host target proteins.

[12493] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM895 gene, herein designated VGAM GENE, on one or more VGAM895 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12494] It is yet further appreciated that a function of VGAM895 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM895 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of



VGAM895 correlate with, and may be deduced from, the identity of the host target genes which VGAM895 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12495] Nucleotide sequences of the VGAM895 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM895 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM895 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM895 are further described hereinbelow with reference to Table 1.

[12496] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM895 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12497] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 896 (VGAM896) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[12498] VGAM896 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM896 was detected is described hereinabove with reference to Figs. 2–8.

[12499] VGAM896 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM896 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12500] VGAM896 gene, herein designated VGAM GENE, encodes a VGAM896 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM896 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM896 precursor RNA is designated SEQ ID:23756, and is provided hereinbelow with reference to the sequence listing part.

[12501] VGAM896 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM896 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12502] An enzyme complex designated DICER COMPLEX, dices the VGAM896 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM896 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM896 RNA is designated SEQ ID:23757, and is provided hereinbelow with reference to the sequence listing part.

[12503] VGAM896 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM896 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM896 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12504] VGAM896 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM896 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM896 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM896 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM896 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12505] The complementary binding of VGAM896 RNA, herein designated VGAM RNA, to host target binding sites on VGAM896 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM896 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM896 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12506] It is appreciated that VGAM896 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM896 host target genes. The mRNA of each one of this plurality of VGAM896 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM896 RNA, herein designated VGAM RNA, and which when bound by VGAM896 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM896 host target proteins.

[12507] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM896 gene, herein designated VGAM GENE, on one or more VGAM896 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12508] It is yet further appreciated that a function of VGAM896 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM896 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM896 correlate with, and may be deduced from, the

identity of the host target genes which VGAM896 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12509] Nucleotide sequences of the VGAM896 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM896 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM896 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM896 are further described hereinbelow with reference to Table 1.

[12510] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM896 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12511] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 897 (VGAM897) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12512] VGAM897 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM897 was detected is described hereinabove with reference to Figs. 2–8.

[12513] VGAM897 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus.

VGAM897 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12514] VGAM897 gene, herein designated VGAM GENE, encodes a VGAM897 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM897 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM897 precursor RNA is designated SEQ ID:23773, and is provided hereinbelow with reference to the sequence listing part.

[12515] VGAM897 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM897 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12516] An enzyme complex designated DICER COMPLEX, dices the VGAM897 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM897 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM897 RNA is designated SEQ ID:23774, and is provided hereinbelow with reference to the sequence listing part.

[12517] VGAM897 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM897 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM897 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12518] VGAM897 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM897 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM897 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM897 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM897 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12519] The complementary binding of VGAM897 RNA, herein designated VGAM RNA, to host target binding sites on VGAM897 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM897 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM897 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12520] It is appreciated that VGAM897 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM897 host target genes. The mRNA of each one of this plurality of VGAM897 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM897 RNA, herein designated VGAM RNA, and which when bound by VGAM897 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM897 host target proteins.

[12521] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM897 gene, herein designated VGAM GENE, on one or more VGAM897 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12522] It is yet further appreciated that a function of VGAM897 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM897 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM897 correlate with, and may be deduced from, the identity of the host target genes which VGAM897 binds and inhibits, and the

function of these host target genes, as elaborated herein—below.

[12523] Nucleotide sequences of the VGAM897 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM897 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM897 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM897 are further described hereinbelow with reference to Table 1.

[12524] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM897 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12525] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 898 (VGAM898) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12526] VGAM898 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM898 was detected is described hereinabove with reference to Figs. 2–8.

[12527] VGAM898 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus.

VGAM898 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12528] VGAM898 gene, herein designated VGAM GENE, encodes a VGAM898 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM898 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM898 precursor RNA is designated SEQ ID:23800, and is provided hereinbelow with reference to the sequence listing part.

[12529] VGAM898 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM898 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12530] An enzyme complex designated DICER COMPLEX, dices the VGAM898 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM898 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM898 RNA is designated SEQ ID:23801, and is provided hereinbelow with reference to the sequence listing part.

[12531] VGAM898 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM898 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM898 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12532] VGAM898 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM898 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM898 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM898 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM898 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[12533] The complementary binding of VGAM898 RNA, herein designated VGAM RNA, to host target binding sites on VGAM898 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM898 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM898 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12534] It is appreciated that VGAM898 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM898 host target genes. The mRNA of each one of this plurality of VGAM898 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM898 RNA, herein designated VGAM RNA, and which when bound by VGAM898 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM898 host target proteins.

[12535] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM898 gene, herein designated VGAM GENE, on one or more VGAM898 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12536] It is yet further appreciated that a function of VGAM898 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM898 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM898 correlate with, and may be deduced from, the identity of the host target genes which VGAM898 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[12537] Nucleotide sequences of the VGAM898 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM898 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM898 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM898 are further described hereinbelow with reference to Table 1.

[12538] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM898 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12539] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 899 (VGAM899) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12540] VGAM899 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM899 was detected is described hereinabove with reference to Figs. 2–8.

[12541] VGAM899 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey astrovirus.

VGAM899 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12542] VGAM899 gene, herein designated VGAM GENE, encodes a VGAM899 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM899 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM899 precursor RNA is designated SEQ ID:23803, and is provided hereinbelow with reference to the sequence listing part.

[12543] VGAM899 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM899 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12544] An enzyme complex designated DICER COMPLEX, dices the VGAM899 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM899 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM899 RNA is designated SEQ ID:23804, and is provided hereinbelow with reference to the sequence listing part.

[12545] VGAM899 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM899 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM899 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[12546] VGAM899 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM899 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM899 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM899 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM899 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12547] The complementary binding of VGAM899 RNA, herein designated VGAM RNA, to host target binding sites on VGAM899 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM899 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM899 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12548] It is appreciated that VGAM899 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM899 host target genes. The mRNA of each one of this plurality of VGAM899 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM899 RNA, herein designated VGAM RNA, and which when bound by VGAM899 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM899 host target proteins.

[12549] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM899 gene, herein designated VGAM GENE, on one or

more VGAM899 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12550] It is yet further appreciated that a function of VGAM899 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM899 include diagnosis, prevention and treatment of viral infection by Turkey astrovirus. Specific functions, and accordingly utilities, of VGAM899 correlate with, and may be deduced from, the identity of the host target genes which VGAM899 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[12551] Nucleotide sequences of the VGAM899 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM899 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM899 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM899 are further described hereinbelow with reference to Table 1.

[12552] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM899 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12553] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 900 (VGAM900) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12554] VGAM900 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM900 was detected is described

hereinabove with reference to Figs. 2–8.

[12555] VGAM900 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM900 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12556] VGAM900 gene, herein designated VGAM GENE, encodes a VGAM900 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM900 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM900 precursor RNA is designated SEQ ID:23810, and is provided hereinbelow with reference to the sequence listing part.

[12557] VGAM900 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM900 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12558] An enzyme complex designated DICER COMPLEX, dices the VGAM900 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM900 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM900 RNA is designated SEQ ID:23811, and is provided hereinbelow with reference to the sequence listing part.

[12559] VGAM900 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM900 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM900 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12560] VGAM900 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM900 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM900 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM900 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM900 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12561] The complementary binding of VGAM900 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM900 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM900 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM900 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12562] It is appreciated that VGAM900 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM900 host target genes. The mRNA of each one of this plurality of VGAM900 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM900 RNA, herein designated VGAM RNA, and which when bound by VGAM900 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM900 host target proteins.

[12563] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM900 gene, herein designated VGAM GENE, on one or more VGAM900 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12564] It is yet further appreciated that a function of VGAM900 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM900 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM900 correlate with, and may be deduced from, the identity of the host target genes which VGAM900 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12565] Nucleotide sequences of the VGAM900 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM900 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM900 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM900 are further described hereinbelow with reference to Table 1.

[12566] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM900 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12567] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 901 (VGAM901) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12568] VGAM901 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM901 was detected is described hereinabove with reference to Figs. 2-8.

[12569] VGAM901 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey astrovirus.

VGAM901 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12570] VGAM901 gene, herein designated VGAM GENE, encodes a VGAM901 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM901 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM901 precursor RNA is designated SEQ ID:23829, and is provided hereinbelow with reference to the sequence listing part.

[12571] VGAM901 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM901 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[12572] An enzyme complex designated DICER COMPLEX, dices the VGAM901 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM901 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM901 RNA is designated SEQ ID:23830, and is provided hereinbelow with reference to the sequence listing part.

[12573] VGAM901 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM901 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM901 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12574] VGAM901 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM901 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM901 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM901 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM901 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12575] The complementary binding of VGAM901 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM901 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM901 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM901 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12576] It is appreciated that VGAM901 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM901 host target genes. The mRNA of each one of this plurality of VGAM901 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM901 RNA, herein designated VGAM RNA, and which when bound by VGAM901 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM901 host target proteins.

[12577] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM901 gene, herein designated VGAM GENE, on one or more VGAM901 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12578] It is yet further appreciated that a function of VGAM901 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM901 include diagnosis, prevention and treatment of viral infection by Turkey astrovirus. Specific functions, and accordingly utilities, of VGAM901 correlate with, and may be deduced from, the identity of the host target genes which VGAM901 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12579] Nucleotide sequences of the VGAM901 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM901 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM901 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM901 are further described hereinbelow with reference to Table 1.

[12580] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM901 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12581] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 902 (VGAM902) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12582] VGAM902 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM902 was detected is described hereinabove with reference to Figs. 2-8.

[12583] VGAM902 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Fowlpox virus.

VGAM902 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12584] VGAM902 gene, herein designated VGAM GENE, encodes a VGAM902 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM902 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM902 precursor RNA is designated SEQ ID:23845, and is provided hereinbelow with reference to the sequence listing part.

[12585] VGAM902 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM902 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12586] An enzyme complex designated DICER COMPLEX, dices the VGAM902 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM902 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM902 RNA is designated SEQ ID:23846, and is provided hereinbelow with reference to the sequence listing part.

[12587] VGAM902 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM902 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM902 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12588] VGAM902 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM902 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM902 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM902 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM902 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12589] The complementary binding of VGAM902 RNA, herein designated VGAM RNA, to host target binding sites on VGAM902 host target RNA, herein designated VGAM HOST



TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM902 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM902 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12590] It is appreciated that VGAM902 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM902 host target genes. The mRNA of each one of this plurality of VGAM902 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM902 RNA, herein designated VGAM RNA, and which when bound by VGAM902 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM902 host target proteins.

[12591] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM902 gene, herein designated VGAM GENE, on one or more VGAM902 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12592] It is yet further appreciated that a function of VGAM902 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM902 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM902 correlate with, and may be deduced from, the identity of the host target genes which VGAM902 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12593] Nucleotide sequences of the VGAM902 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM902 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM902 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM902 are further described hereinbelow with reference to Table 1.

[12594] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM902 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12595] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 903 (VGAM903) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12596] VGAM903 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM903 was detected is described hereinabove with reference to Figs. 2-8.

[12597] VGAM903 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM903 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12598] VGAM903 gene, herein designated VGAM GENE, encodes a VGAM903 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM903 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM903 precursor RNA is designated SEQ ID:23850, and is provided hereinbelow with reference to the sequence listing part.

[12599] VGAM903 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM903 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12600] An enzyme complex designated DICER COMPLEX, dices

the VGAM903 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM903 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM903 RNA is designated SEQ ID:23851, and is provided hereinbelow with reference to the sequence listing part.

[12601] VGAM903 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM903 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM903 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12602] VGAM903 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM903 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM903 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM903 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM903 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12603] The complementary binding of VGAM903 RNA, herein designated VGAM RNA, to host target binding sites on VGAM903 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM903 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM903 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12604] It is appreciated that VGAM903 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM903 host target genes. The mRNA of each one of this plurality of VGAM903 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM903 RNA, herein designated VGAM RNA, and which when bound by VGAM903 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM903 host target proteins.

[12605] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM903 gene, herein designated VGAM GENE, on one or more VGAM903 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12606] It is yet further appreciated that a function of VGAM903 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM903 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM903 correlate with, and may be deduced from, the identity of the host target genes which VGAM903 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12607] Nucleotide sequences of the VGAM903 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM903 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM903 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM903 are further described hereinbelow with reference to Table 1.

[12608] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM903 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12609] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 904 (VGAM904) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12610] VGAM904 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM904 was detected is described hereinabove with reference to Figs. 2-8.

[12611] VGAM904 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM904 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[12612] VGAM904 gene, herein designated VGAM GENE, encodes a VGAM904 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM904 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM904 precursor RNA is designated SEQ ID:23861, and is provided hereinbelow with reference to the sequence listing part.

[12613] VGAM904 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM904 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12614] An enzyme complex designated DICER COMPLEX, dices the VGAM904 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM904 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM904 RNA is designated SEQ ID:23862, and is provided hereinbelow with reference to the sequence listing part.

[12615] VGAM904 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM904 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM904 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12616] VGAM904 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM904 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM904 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM904 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM904 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12617] The complementary binding of VGAM904 RNA, herein designated VGAM RNA, to host target binding sites on VGAM904 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM904 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM904 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12618] It is appreciated that VGAM904 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM904 host target genes. The mRNA of each one of this plurality of VGAM904 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM904 RNA, herein designated VGAM RNA, and which when bound by VGAM904 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM904 host target proteins.

[12619] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM904 gene, herein designated VGAM GENE, on one or more VGAM904 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12620] It is yet further appreciated that a function of VGAM904 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM904 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM904 correlate with, and may be deduced from, the identity of the host target genes which VGAM904 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12621] Nucleotide sequences of the VGAM904 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM904 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM904 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM904 are further described hereinbelow with reference to Table 1.

[12622] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM904 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12623] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 905 (VGAM905) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12624] VGAM905 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM905 was detected is described hereinabove with reference to Figs. 2-8.

[12625] VGAM905 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM905 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[12626] VGAM905 gene, herein designated VGAM GENE, encodes a VGAM905 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM905 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM905 precursor RNA is designated SEQ ID:23882, and is provided hereinbelow with reference to the sequence listing part.

[12627] VGAM905 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM905 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12628] An enzyme complex designated DICER COMPLEX, dices the VGAM905 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM905 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM905 RNA is designated SEQ ID:23883, and is provided hereinbelow with reference to the sequence listing part.

[12629] VGAM905 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM905 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM905 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12630] VGAM905 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM905 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM905 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM905 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM905 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12631] The complementary binding of VGAM905 RNA, herein designated VGAM RNA, to host target binding sites on VGAM905 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM905 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM905 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12632] It is appreciated that VGAM905 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM905 host target genes. The mRNA of each one of this plurality of VGAM905 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM905 RNA, herein designated VGAM RNA, and which when bound by VGAM905 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM905 host target proteins.

[12633] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM905 gene, herein designated VGAM GENE, on one or more VGAM905 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12634] It is yet further appreciated that a function of VGAM905 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM905 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM905 correlate with, and may be deduced from, the identity of the host target genes which VGAM905 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12635] Nucleotide sequences of the VGAM905 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM905 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM905 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM905 are further de-

scribed hereinbelow with reference to Table 1.

[12636] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM905 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12637] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 906 (VGAM906) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12638] VGAM906 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM906 was detected is described hereinabove with reference to Figs. 2-8.

[12639] VGAM906 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM906 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12640] VGAM906 gene, herein designated VGAM GENE, encodes a VGAM906 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM906 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM906 precursor RNA is designated SEQ ID:23888, and is provided hereinbelow with reference to the sequence listing part.

[12641] VGAM906 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM906 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12642] An enzyme complex designated DICER COMPLEX, dices the VGAM906 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM906 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM906 RNA is designated SEQ ID:23889, and is provided hereinbelow with reference to the sequence listing part.

[12643] VGAM906 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM906 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM906 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12644] VGAM906 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM906 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM906 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM906 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM906 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12645] The complementary binding of VGAM906 RNA, herein designated VGAM RNA, to host target binding sites on VGAM906 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM906 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM906 host target protein, herein designated



VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12646] It is appreciated that VGAM906 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM906 host target genes. The mRNA of each one of this plurality of VGAM906 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM906 RNA, herein designated VGAM RNA, and which when bound by VGAM906 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM906 host target proteins.

[12647] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM906 gene, herein designated VGAM GENE, on one or more VGAM906 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12648] It is yet further appreciated that a function of VGAM906 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM906 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM906 correlate with, and may be deduced from, the identity of the host target genes which VGAM906 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12649] Nucleotide sequences of the VGAM906 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM906 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM906 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM906 are further described hereinbelow with reference to Table 1.

[12650] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM906 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12651] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 907 (VGAM907) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12652] VGAM907 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM907 was detected is described hereinabove with reference to Figs. 2-8.

[12653] VGAM907 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM907 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12654] VGAM907 gene, herein designated VGAM GENE, encodes a

VGAM907 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM907 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM907 precursor RNA is designated SEQ ID:23905, and is provided hereinbelow with reference to the sequence listing part.

[12655] VGAM907 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM907 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12656] An enzyme complex designated DICER COMPLEX, dices the VGAM907 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM907 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM907 RNA is designated SEQ ID:23906, and is provided hereinbelow with reference to the sequence listing part.

[12657] VGAM907 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM907 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM907 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12658] VGAM907 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM907 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM907 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM907 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM907 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12659] The complementary binding of VGAM907 RNA, herein designated VGAM RNA, to host target binding sites on VGAM907 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM907 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM907 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[12660] It is appreciated that VGAM907 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM907 host target genes. The mRNA of each one of this plurality of VGAM907 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM907 RNA, herein designated VGAM RNA, and which when bound by VGAM907 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM907 host target proteins.

[12661] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM907 gene, herein designated VGAM GENE, on one or more VGAM907 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12662] It is yet further appreciated that a function of VGAM907 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM907 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM907 correlate with, and may be deduced from, the identity of the host target genes which VGAM907 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12663] Nucleotide sequences of the VGAM907 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM907 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM907 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM907 are further described hereinbelow with reference to Table 1.

[12664] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM907 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12665] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 908 (VGAM908) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12666] VGAM908 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM908 was detected is described hereinabove with reference to Figs. 2-8.

[12667] VGAM908 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM908 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12668] VGAM908 gene, herein designated VGAM GENE, encodes a VGAM908 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM908 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM908 precursor RNA is designated SEQ ID:23913, and is provided hereinbelow with reference to the sequence listing part.

[12669] VGAM908 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM908 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12670] An enzyme complex designated DICER COMPLEX, dices the VGAM908 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM908 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM908 RNA is designated SEQ ID:23914, and is provided hereinbelow with reference to the sequence listing part.

[12671] VGAM908 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM908 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM908 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12672] VGAM908 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM908 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM908 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM908 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM908 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12673] The complementary binding of VGAM908 RNA, herein designated VGAM RNA, to host target binding sites on VGAM908 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM908 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM908 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12674] It is appreciated that VGAM908 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM908 host target genes. The mRNA of each one of this plurality of VGAM908 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM908 RNA, herein designated VGAM RNA, and which when bound by VGAM908 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM908 host target proteins.

[12675] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM908 gene, herein designated VGAM GENE, on one or more VGAM908 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12676] It is yet further appreciated that a function of VGAM908 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM908 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM908 correlate with, and may be deduced from, the identity of the host target genes which VGAM908 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12677] Nucleotide sequences of the VGAM908 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM908 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM908 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM908 are further described hereinbelow with reference to Table 1.

[12678] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM908 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12679] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 909 (VGAM909) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12680] VGAM909 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM909 was detected is described hereinabove with reference to Figs. 2–8.

[12681] VGAM909 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM909 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12682] VGAM909 gene, herein designated VGAM GENE, encodes a VGAM909 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM909 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM909 precursor RNA is designated SEQ ID:23917, and is provided hereinbelow with reference to the sequence listing part.

[12683] VGAM909 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM909 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12684] An enzyme complex designated DICER COMPLEX, dices the VGAM909 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM909 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM909 RNA is designated SEQ ID:23918, and is provided hereinbelow with reference to the sequence listing part.

[12685] VGAM909 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM909 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM909 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12686] VGAM909 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM909 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM909 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM909 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM909 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12687] The complementary binding of VGAM909 RNA, herein designated VGAM RNA, to host target binding sites on VGAM909 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM909 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM909 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12688] It is appreciated that VGAM909 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM909 host target genes. The mRNA of each one of this plurality of VGAM909 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM909 RNA, herein designated VGAM RNA, and which when bound by VGAM909 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM909 host target proteins.

[12689] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM909 gene, herein designated VGAM GENE, on one or more VGAM909 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12690] It is yet further appreciated that a function of VGAM909 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM909 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM909 correlate with, and may be deduced from, the identity of the host target genes which VGAM909 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12691] Nucleotide sequences of the VGAM909 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM909 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM909 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM909 are further described hereinbelow with reference to Table 1.

[12692] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM909 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12693] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 910 (VGAM910) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12694] VGAM910 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM910 was detected is described hereinabove with reference to Figs. 2–8.

[12695] VGAM910 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM910 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12696] VGAM910 gene, herein designated VGAM GENE, encodes a VGAM910 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM910 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM910 precursor RNA is designated SEQ ID:23926, and is provided hereinbelow with reference to the sequence listing part.

[12697] VGAM910 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM910 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12698] An enzyme complex designated DICER COMPLEX, dices the VGAM910 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM910 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM910 RNA is designated SEQ ID:23927, and is provided hereinbelow with reference to the sequence listing part.

[12699] VGAM910 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM910 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM910 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12700] VGAM910 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM910 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM910 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM910 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM910 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12701] The complementary binding of VGAM910 RNA, herein designated VGAM RNA, to host target binding sites on VGAM910 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM910 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM910 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12702] It is appreciated that VGAM910 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM910 host target genes. The mRNA of each one of this plurality of VGAM910 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM910 RNA, herein designated VGAM RNA, and which when bound by VGAM910 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM910 host target proteins.

[12703] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM910 gene, herein designated VGAM GENE, on one or more VGAM910 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[12704] It is yet further appreciated that a function of VGAM910 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM910 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM910 correlate with, and may be deduced from, the identity of the host target genes which VGAM910 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[12705] Nucleotide sequences of the VGAM910 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM910 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM910 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM910 are further described hereinbelow with reference to Table 1.

[12706] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM910 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12707] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 911 (VGAM911) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12708] VGAM911 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM911 was detected is described hereinabove with reference to Figs. 2–8.

[12709] VGAM911 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM911 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12710] VGAM911 gene, herein designated VGAM GENE, encodes a VGAM911 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM911 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM911 precursor RNA is designated SEQ ID:23946, and is provided hereinbelow with reference to the sequence listing part.

[12711] VGAM911 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM911 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12712] An enzyme complex designated DICER COMPLEX, dices the VGAM911 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM911 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM911 RNA is designated SEQ ID:23947, and is provided hereinbelow with reference to the sequence listing part.

[12713] VGAM911 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM911 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM911 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12714] VGAM911 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM911 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM911 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM911 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM911 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12715] The complementary binding of VGAM911 RNA, herein designated VGAM RNA, to host target binding sites on VGAM911 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM911 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM911 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12716] It is appreciated that VGAM911 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM911 host target genes. The mRNA of

each one of this plurality of VGAM911 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM911 RNA, herein designated VGAM RNA, and which when bound by VGAM911 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM911 host target proteins.

[12717] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM911 gene, herein designated VGAM GENE, on one or more VGAM911 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[12718] It is yet further appreciated that a function of VGAM911 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM911 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM911 correlate with, and may be deduced from, the identity of the host target genes which VGAM911 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12719] Nucleotide sequences of the VGAM911 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM911 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM911 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM911 are further described hereinbelow with reference to Table 1.

[12720] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM911 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[12721] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 912 (VGAM912) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12722] VGAM912 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM912 was detected is described hereinabove with reference to Figs. 2–8.

[12723] VGAM912 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM912 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12724] VGAM912 gene, herein designated VGAM GENE, encodes a VGAM912 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM912 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM912 precursor RNA is designated SEQ ID:23958, and is provided hereinbelow with reference to the sequence listing part.

[12725] VGAM912 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM912 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12726] An enzyme complex designated DICER COMPLEX, dices the VGAM912 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM912 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM912 RNA is designated SEQ ID:23959, and

is provided hereinbelow with reference to the sequence listing part.

[12727] VGAM912 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM912 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM912 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12728] VGAM912 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM912 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM912 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM912 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM912 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12729] The complementary binding of VGAM912 RNA, herein designated VGAM RNA, to host target binding sites on VGAM912 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM912 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM912 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12730] It is appreciated that VGAM912 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM912 host target genes. The mRNA of each one of this plurality of VGAM912 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM912 RNA, herein designated VGAM RNA, and which when bound by VGAM912 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM912 host target proteins.

[12731] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM912 gene, herein designated VGAM GENE, on one or more VGAM912 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12732] It is yet further appreciated that a function of VGAM912 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM912 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM912 correlate with, and may be deduced from, the identity of the host target genes which VGAM912 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12733] Nucleotide sequences of the VGAM912 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM912 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM912 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM912 are further described hereinbelow with reference to Table 1.

[12734] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM912 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12735] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 913 (VGAM913) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12736] VGAM913 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM913 was detected is described hereinabove with reference to Figs. 2–8.

[12737] VGAM913 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM913 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12738] VGAM913 gene, herein designated VGAM GENE, encodes a VGAM913 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM913 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM913 precursor RNA is

designated SEQ ID:23964, and is provided hereinbelow with reference to the sequence listing part.

[12739] VGAM913 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM913 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12740] An enzyme complex designated DICER COMPLEX, dices the VGAM913 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM913 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM913 RNA is designated SEQ ID:23965, and is provided hereinbelow with reference to the sequence



listing part.

[12741] VGAM913 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM913 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM913 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12742] VGAM913 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM913 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM913 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM913 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM913 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12743] The complementary binding of VGAM913 RNA, herein designated VGAM RNA, to host target binding sites on VGAM913 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM913 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM913 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12744] It is appreciated that VGAM913 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM913 host target genes. The mRNA of each one of this plurality of VGAM913 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM913 RNA, herein designated VGAM RNA, and which when bound by VGAM913 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM913 host target proteins.

[12745] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM913 gene, herein designated VGAM GENE, on one or more VGAM913 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12746] It is yet further appreciated that a function of VGAM913 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM913 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM913 correlate with, and may be deduced from, the identity of the host target genes which VGAM913 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12747] Nucleotide sequences of the VGAM913 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM913 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM913 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM913 are further described hereinbelow with reference to Table 1.

[12748] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM913 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12749] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 914 (VGAM914) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12750] VGAM914 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM914 was detected is described hereinabove with reference to Figs. 2–8.

[12751] VGAM914 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM914 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12752] VGAM914 gene, herein designated VGAM GENE, encodes a VGAM914 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM914 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM914 precursor RNA is designated SEQ ID:23969, and is provided hereinbelow

with reference to the sequence listing part.

[12753] VGAM914 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM914 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12754] An enzyme complex designated DICER COMPLEX, dices the VGAM914 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM914 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM914 RNA is designated SEQ ID:23970, and is provided hereinbelow with reference to the sequence listing part.

[12755] VGAM914 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM914 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM914 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12756] VGAM914 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM914 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM914 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM914 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM914 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12757] The complementary binding of VGAM914 RNA, herein designated VGAM RNA, to host target binding sites on VGAM914 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM914 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM914 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12758] It is appreciated that VGAM914 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM914 host target genes. The mRNA of each one of this plurality of VGAM914 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM914 RNA, herein designated VGAM RNA, and which when bound by VGAM914 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM914 host target proteins.

[12759] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM914 gene, herein designated VGAM GENE, on one or more VGAM914 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12760] It is yet further appreciated that a function of VGAM914 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM914 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM914 correlate with, and may be deduced from, the identity of the host target genes which VGAM914 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12761] Nucleotide sequences of the VGAM914 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM914 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM914 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM914 are further described hereinbelow with reference to Table 1.

[12762] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM914 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12763] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 915 (VGAM915) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12764] VGAM915 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM915 was detected is described hereinabove with reference to Figs. 2–8.

[12765] VGAM915 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM915 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12766] VGAM915 gene, herein designated VGAM GENE, encodes a VGAM915 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM915 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM915 precursor RNA is designated SEQ ID:23974, and is provided hereinbelow with reference to the sequence listing part.

[12767] VGAM915 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM915 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12768] An enzyme complex designated DICER COMPLEX, dices the VGAM915 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM915 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM915 RNA is designated SEQ ID:23975, and is provided hereinbelow with reference to the sequence listing part.

[12769] VGAM915 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM915 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM915 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12770] VGAM915 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM915 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM915 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM915 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM915 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12771] The complementary binding of VGAM915 RNA, herein designated VGAM RNA, to host target binding sites on VGAM915 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM915 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM915 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12772] It is appreciated that VGAM915 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM915 host target genes. The mRNA of each one of this plurality of VGAM915 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM915 RNA, herein designated VGAM

RNA, and which when bound by VGAM915 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM915 host target proteins.

[12773] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM915 gene, herein designated VGAM GENE, on one or more VGAM915 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12774] It is yet further appreciated that a function of VGAM915 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM915 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM915 correlate with, and may be deduced from, the identity of the host target genes which VGAM915 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12775] Nucleotide sequences of the VGAM915 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM915 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM915 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM915 are further described hereinbelow with reference to Table 1.

[12776] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM915 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12777] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 916 (VGAM916) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12778] VGAM916 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM916 was detected is described hereinabove with reference to Figs. 2–8.

[12779] VGAM916 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM916 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12780] VGAM916 gene, herein designated VGAM GENE, encodes a VGAM916 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM916 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM916 precursor RNA is designated SEQ ID:23987, and is provided hereinbelow with reference to the sequence listing part.

[12781] VGAM916 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM916 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12782] An enzyme complex designated DICER COMPLEX, dices the VGAM916 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM916 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM916 RNA is designated SEQ ID:23988, and is provided hereinbelow with reference to the sequence listing part.

[12783] VGAM916 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM916 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM916 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12784] VGAM916 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM916 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM916 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM916 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM916 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12785] The complementary binding of VGAM916 RNA, herein designated VGAM RNA, to host target binding sites on VGAM916 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM916 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM916 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12786] It is appreciated that VGAM916 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM916 host target genes. The mRNA of each one of this plurality of VGAM916 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM916 RNA, herein designated VGAM RNA, and which when bound by VGAM916 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM916 host target proteins.

[12787] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM916 gene, herein designated VGAM GENE, on one or more VGAM916 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12788] It is yet further appreciated that a function of VGAM916 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM916 include diagnosis, prevention and

treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM916 correlate with, and may be deduced from, the identity of the host target genes which VGAM916 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12789] Nucleotide sequences of the VGAM916 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM916 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM916 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM916 are further described hereinbelow with reference to Table 1.

[12790] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM916 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12791] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 917 (VGAM917) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12792] VGAM917 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM917 was detected is described hereinabove with reference to Figs. 2–8.

[12793] VGAM917 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM917 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12794] VGAM917 gene, herein designated VGAM GENE, encodes a VGAM917 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM917 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM917 precursor RNA is designated SEQ ID:24000, and is provided hereinbelow with reference to the sequence listing part.

[12795] VGAM917 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM917 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12796] An enzyme complex designated DICER COMPLEX, dices the VGAM917 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM917 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM917 RNA is designated SEQ ID:24001, and is provided hereinbelow with reference to the sequence listing part.

[12797] VGAM917 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM917 host target RNA, herein designated VGAM



HOST TARGET RNA. VGAM917 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12798] VGAM917 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM917 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM917 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM917 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM917 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12799] The complementary binding of VGAM917 RNA, herein designated VGAM RNA, to host target binding sites on VGAM917 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM917 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM917 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12800] It is appreciated that VGAM917 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM917 host target genes. The mRNA of each one of this plurality of VGAM917 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM917 RNA, herein designated VGAM RNA, and which when bound by VGAM917 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM917 host target proteins.

[12801] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM917 gene, herein designated VGAM GENE, on one or more VGAM917 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12802] It is yet further appreciated that a function of VGAM917 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM917 include diagnosis, prevention and treatment of viral infection by Chimpanzee cy-

tomegalovirus. Specific functions, and accordingly utilities, of VGAM917 correlate with, and may be deduced from, the identity of the host target genes which VGAM917 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12803] Nucleotide sequences of the VGAM917 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM917 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM917 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM917 are further described hereinbelow with reference to Table 1.

[12804] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM917 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12805] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 918 (VGAM918) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[12806] VGAM918 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM918 was detected is described hereinabove with reference to Figs. 2–8.

[12807] VGAM918 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM918 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12808] VGAM918 gene, herein designated VGAM GENE, encodes a VGAM918 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM918 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM918 precursor RNA is designated SEQ ID:24004, and is provided hereinbelow with reference to the sequence listing part.

[12809] VGAM918 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM918 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12810] An enzyme complex designated DICER COMPLEX, dices the VGAM918 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM918 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM918 RNA is designated SEQ ID:24005, and is provided hereinbelow with reference to the sequence listing part.

[12811] VGAM918 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM918 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM918 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12812] VGAM918 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM918 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM918 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM918 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM918 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12813] The complementary binding of VGAM918 RNA, herein designated VGAM RNA, to host target binding sites on VGAM918 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM918 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM918 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12814] It is appreciated that VGAM918 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM918 host target genes. The mRNA of each one of this plurality of VGAM918 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM918 RNA, herein designated VGAM RNA, and which when bound by VGAM918 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM918 host target proteins.



[12815] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM918 gene, herein designated VGAM GENE, on one or more VGAM918 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12816] It is yet further appreciated that a function of VGAM918 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM918 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utili-

ties, of VGAM918 correlate with, and may be deduced from, the identity of the host target genes which VGAM918 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12817] Nucleotide sequences of the VGAM918 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM918 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM918 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM918 are further described hereinbelow with reference to Table 1.

[12818] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM918 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12819] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 919 (VGAM919) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[12820] VGAM919 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM919 was detected is described hereinabove with reference to Figs. 2–8.

[12821] VGAM919 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM919 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12822] VGAM919 gene, herein designated VGAM GENE, encodes a VGAM919 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM919 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM919 precursor RNA is designated SEQ ID:24008, and is provided hereinbelow with reference to the sequence listing part.

[12823] VGAM919 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM919 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12824] An enzyme complex designated DICER COMPLEX, dices the VGAM919 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM919 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM919 RNA is designated SEQ ID:24009, and is provided hereinbelow with reference to the sequence listing part.

[12825] VGAM919 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM919 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM919 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12826] VGAM919 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM919 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM919 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM919 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM919 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12827] The complementary binding of VGAM919 RNA, herein designated VGAM RNA, to host target binding sites on VGAM919 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM919 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM919 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12828] It is appreciated that VGAM919 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM919 host target genes. The mRNA of each one of this plurality of VGAM919 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM919 RNA, herein designated VGAM RNA, and which when bound by VGAM919 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM919 host target proteins.

[12829] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM919 gene, herein designated VGAM GENE, on one or more VGAM919 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12830] It is yet further appreciated that a function of VGAM919 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM919 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM919 correlate with, and may be deduced

from, the identity of the host target genes which VGAM919 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12831] Nucleotide sequences of the VGAM919 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM919 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM919 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM919 are further described hereinbelow with reference to Table 1.

[12832] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM919 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12833] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 920 (VGAM920) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[12834] VGAM920 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM920 was detected is described hereinabove with reference to Figs. 2–8.

[12835] VGAM920 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM920 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12836] VGAM920 gene, herein designated VGAM GENE, encodes a VGAM920 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM920 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM920 precursor RNA is designated SEQ ID:24012, and is provided hereinbelow with reference to the sequence listing part.

[12837] VGAM920 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM920 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12838] An enzyme complex designated DICER COMPLEX, dices the VGAM920 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM920 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM920 RNA is designated SEQ ID:24013, and is provided hereinbelow with reference to the sequence listing part.

[12839] VGAM920 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM920 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM920 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12840] VGAM920 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM920 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM920 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM920 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM920 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12841] The complementary binding of VGAM920 RNA, herein designated VGAM RNA, to host target binding sites on VGAM920 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM920 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM920 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12842] It is appreciated that VGAM920 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM920 host target genes. The mRNA of each one of this plurality of VGAM920 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM920 RNA, herein designated VGAM RNA, and which when bound by VGAM920 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM920 host target proteins.

[12843] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM920 gene, herein designated VGAM GENE, on one or more VGAM920 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12844] It is yet further appreciated that a function of VGAM920 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM920 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM920 correlate with, and may be deduced from, the identity of the host target genes which

VGAM920 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12845] Nucleotide sequences of the VGAM920 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM920 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM920 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM920 are further described hereinbelow with reference to Table 1.

[12846] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM920 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12847] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 921 (VGAM921) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12848] VGAM921 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM921 was detected is described hereinabove with reference to Figs. 2–8.

[12849] VGAM921 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM921 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12850] VGAM921 gene, herein designated VGAM GENE, encodes a VGAM921 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM921 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM921 precursor RNA is designated SEQ ID:24015, and is provided hereinbelow with reference to the sequence listing part.

[12851] VGAM921 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM921 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12852] An enzyme complex designated DICER COMPLEX, dices the VGAM921 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM921 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM921 RNA is designated SEQ ID:24016, and is provided hereinbelow with reference to the sequence listing part.

[12853] VGAM921 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM921 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM921 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12854] VGAM921 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM921 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM921 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM921 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM921 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3'UTR and 5'UTR regions.

[12855] The complementary binding of VGAM921 RNA, herein designated VGAM RNA, to host target binding sites on VGAM921 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM921 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM921 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12856] It is appreciated that VGAM921 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM921 host target genes. The mRNA of each one of this plurality of VGAM921 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM921 RNA, herein designated VGAM RNA, and which when bound by VGAM921 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM921 host target proteins.

[12857] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM921 gene, herein designated VGAM GENE, on one or more VGAM921 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12858] It is yet further appreciated that a function of VGAM921 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM921 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utilities, of VGAM921 correlate with, and may be deduced from, the identity of the host target genes which VGAM921 binds and inhibits, and the function of these

host target genes, as elaborated hereinbelow.

[12859] Nucleotide sequences of the VGAM921 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM921 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM921 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM921 are further described hereinbelow with reference to Table 1.

[12860] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM921 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12861] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 922 (VGAM922) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12862] VGAM922 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM922 was detected is described hereinabove with reference to Figs. 2–8.

[12863] VGAM922 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline foamy virus.

VGAM922 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12864] VGAM922 gene, herein designated VGAM GENE, encodes a VGAM922 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM922 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM922 precursor RNA is designated SEQ ID:24045, and is provided hereinbelow with reference to the sequence listing part.

[12865] VGAM922 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM922 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12866] An enzyme complex designated DICER COMPLEX, dices the VGAM922 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM922 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM922 RNA is designated SEQ ID:24046, and is provided hereinbelow with reference to the sequence listing part.

[12867] VGAM922 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM922 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM922 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[12868] VGAM922 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM922 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM922 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM922 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM922 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12869] The complementary binding of VGAM922 RNA, herein designated VGAM RNA, to host target binding sites on VGAM922 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM922 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM922 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12870] It is appreciated that VGAM922 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM922 host target genes. The mRNA of each one of this plurality of VGAM922 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM922 RNA, herein designated VGAM RNA, and which when bound by VGAM922 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM922 host target proteins.

[12871] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM922 gene, herein designated VGAM GENE, on one or



more VGAM922 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12872] It is yet further appreciated that a function of VGAM922 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM922 include diagnosis, prevention and treatment of viral infection by Feline foamy virus. Specific functions, and accordingly utilities, of VGAM922 correlate with, and may be deduced from, the identity of the host target genes which VGAM922 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12873] Nucleotide sequences of the VGAM922 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM922 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM922 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM922 are further described hereinbelow with reference to Table 1.

[12874] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM922 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12875] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 923 (VGAM923) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12876] VGAM923 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM923 was detected is described

hereinabove with reference to Figs. 2–8.

[12877] VGAM923 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM923 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12878] VGAM923 gene, herein designated VGAM GENE, encodes a VGAM923 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM923 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM923 precursor RNA is designated SEQ ID:24066, and is provided hereinbelow with reference to the sequence listing part.

[12879] VGAM923 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM923 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12880] An enzyme complex designated DICER COMPLEX, dices the VGAM923 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM923 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM923 RNA is designated SEQ ID:24067, and is provided hereinbelow with reference to the sequence listing part.

[12881] VGAM923 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM923 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM923 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12882] VGAM923 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM923 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM923 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM923 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM923 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12883] The complementary binding of VGAM923 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM923 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM923 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM923 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12884] It is appreciated that VGAM923 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM923 host target genes. The mRNA of each one of this plurality of VGAM923 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM923 RNA, herein designated VGAM RNA, and which when bound by VGAM923 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM923 host target proteins.

[12885] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM923 gene, herein designated VGAM GENE, on one or more VGAM923 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12886] It is yet further appreciated that a function of VGAM923 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM923 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM923 correlate with, and may be deduced from, the identity of the host target genes which VGAM923 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12887] Nucleotide sequences of the VGAM923 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM923 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM923 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM923 are further described hereinbelow with reference to Table 1.

[12888] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM923 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12889] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 924 (VGAM924) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12890] VGAM924 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM924 was detected is described hereinabove with reference to Figs. 2-8.



[12891] VGAM924 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM924 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12892] VGAM924 gene, herein designated VGAM GENE, encodes a VGAM924 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM924 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM924 precursor RNA is designated SEQ ID:24075, and is provided hereinbelow with reference to the sequence listing part.

[12893] VGAM924 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM924 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[12894] An enzyme complex designated DICER COMPLEX, dices the VGAM924 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM924 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM924 RNA is designated SEQ ID:24076, and is provided hereinbelow with reference to the sequence listing part.

[12895] VGAM924 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM924 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM924 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12896] VGAM924 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM924 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM924 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM924 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM924 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12897] The complementary binding of VGAM924 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM924 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM924 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM924 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12898] It is appreciated that VGAM924 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM924 host target genes. The mRNA of each one of this plurality of VGAM924 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM924 RNA, herein designated VGAM RNA, and which when bound by VGAM924 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM924 host target proteins.

[12899] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM924 gene, herein designated VGAM GENE, on one or more VGAM924 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12900] It is yet further appreciated that a function of VGAM924 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM924 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM924 correlate with, and may be deduced from, the identity of the host target genes which VGAM924 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12901] Nucleotide sequences of the VGAM924 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM924 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM924 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM924 are further described hereinbelow with reference to Table 1.

[12902] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM924 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12903] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 925 (VGAM925) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12904] VGAM925 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM925 was detected is described hereinabove with reference to Figs. 2-8.

[12905] VGAM925 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Murine adenovirus A. VGAM925 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12906] VGAM925 gene, herein designated VGAM GENE, encodes a VGAM925 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM925 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM925 precursor RNA is designated SEQ ID:24092, and is provided hereinbelow with reference to the sequence listing part.

[12907] VGAM925 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM925 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12908] An enzyme complex designated DICER COMPLEX, dices the VGAM925 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM925 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM925 RNA is designated SEQ ID:24093, and is provided hereinbelow with reference to the sequence listing part.

[12909] VGAM925 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM925 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM925 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12910] VGAM925 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM925 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM925 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM925 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM925 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12911] The complementary binding of VGAM925 RNA, herein designated VGAM RNA, to host target binding sites on VGAM925 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM925 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM925 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12912] It is appreciated that VGAM925 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM925 host target genes. The mRNA of each one of this plurality of VGAM925 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM925 RNA, herein designated VGAM RNA, and which when bound by VGAM925 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM925 host target proteins.

[12913] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM925 gene, herein designated VGAM GENE, on one or more VGAM925 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12914] It is yet further appreciated that a function of VGAM925 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM925 include diagnosis, prevention and treatment of viral infection by Murine adenovirus A. Specific functions, and accordingly utilities, of VGAM925 correlate with, and may be deduced from, the identity of the host target genes which VGAM925 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12915] Nucleotide sequences of the VGAM925 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM925 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM925 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM925 are further described hereinbelow with reference to Table 1.

[12916] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM925 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12917] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 926 (VGAM926) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12918] VGAM926 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM926 was detected is described hereinabove with reference to Figs. 2-8.

[12919] VGAM926 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey adenovirus 3.

VGAM926 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12920] VGAM926 gene, herein designated VGAM GENE, encodes a VGAM926 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM926 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM926 precursor RNA is designated SEQ ID:24097, and is provided hereinbelow with reference to the sequence listing part.

[12921] VGAM926 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM926 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12922] An enzyme complex designated DICER COMPLEX, dices

the VGAM926 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM926 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM926 RNA is designated SEQ ID:24098, and is provided hereinbelow with reference to the sequence listing part.

[12923] VGAM926 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM926 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM926 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12924] VGAM926 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM926 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM926 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM926 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM926 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12925] The complementary binding of VGAM926 RNA, herein designated VGAM RNA, to host target binding sites on VGAM926 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM926 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM926 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12926] It is appreciated that VGAM926 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM926 host target genes. The mRNA of each one of this plurality of VGAM926 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM926 RNA, herein designated VGAM RNA, and which when bound by VGAM926 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM926 host target proteins.

[12927] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM926 gene, herein designated VGAM GENE, on one or more VGAM926 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12928] It is yet further appreciated that a function of VGAM926 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM926 include diagnosis, prevention and treatment of viral infection by Turkey adenovirus 3. Specific functions, and accordingly utilities, of VGAM926 correlate with, and may be deduced from, the identity of the host target genes which VGAM926 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12929] Nucleotide sequences of the VGAM926 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM926 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM926 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM926 are further described hereinbelow with reference to Table 1.

[12930] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM926 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12931] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 927 (VGAM927) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12932] VGAM927 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM927 was detected is described hereinabove with reference to Figs. 2-8.

[12933] VGAM927 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murine adenovirus A. VGAM927 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[12934] VGAM927 gene, herein designated VGAM GENE, encodes a VGAM927 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM927 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM927 precursor RNA is designated SEQ ID:24100, and is provided hereinbelow with reference to the sequence listing part.

[12935] VGAM927 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM927 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12936] An enzyme complex designated DICER COMPLEX, dices the VGAM927 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM927 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM927 RNA is designated SEQ ID:24101, and is provided hereinbelow with reference to the sequence listing part.

[12937] VGAM927 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM927 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM927 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12938] VGAM927 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM927 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM927 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM927 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12939] The complementary binding of VGAM927 RNA, herein designated VGAM RNA, to host target binding sites on VGAM927 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM927 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM927 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12940] It is appreciated that VGAM927 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM927 host target genes. The mRNA of each one of this plurality of VGAM927 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM927 RNA, herein designated VGAM RNA, and which when bound by VGAM927 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM927 host target proteins.

[12941] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM927 gene, herein designated VGAM GENE, on one or more VGAM927 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12942] It is yet further appreciated that a function of VGAM927 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of viral infection by Murine adenovirus A. Specific functions, and accordingly utilities, of VGAM927 correlate with, and may be deduced from, the identity of the host target genes which VGAM927 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12943] Nucleotide sequences of the VGAM927 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM927 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM927 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM927 are further described hereinbelow with reference to Table 1.

[12944] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM927 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12945] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 928 (VGAM928) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12946] VGAM928 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM928 was detected is described hereinabove with reference to Figs. 2-8.

[12947] VGAM928 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Odontoglossum ringspot virus. VGAM928 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in



the human genome.

[12948] VGAM928 gene, herein designated VGAM GENE, encodes a VGAM928 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM928 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM928 precursor RNA is designated SEQ ID:24154, and is provided hereinbelow with reference to the sequence listing part.

[12949] VGAM928 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM928 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12950] An enzyme complex designated DICER COMPLEX, dices the VGAM928 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM928 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM928 RNA is designated SEQ ID:24155, and is provided hereinbelow with reference to the sequence listing part.

[12951] VGAM928 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12952] VGAM928 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM928 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM928 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12953] The complementary binding of VGAM928 RNA, herein designated VGAM RNA, to host target binding sites on VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM928 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12954] It is appreciated that VGAM928 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM928 host target genes. The mRNA of each one of this plurality of VGAM928 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM928 RNA, herein designated VGAM RNA, and which when bound by VGAM928 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM928 host target proteins.

[12955] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM928 gene, herein designated VGAM GENE, on one or more VGAM928 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12956] It is yet further appreciated that a function of VGAM928 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM928 include diagnosis, prevention and treatment of viral infection by Odontoglossum ringspot virus. Specific functions, and accordingly utilities, of VGAM928 correlate with, and may be deduced from, the identity of the host target genes which VGAM928 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12957] Nucleotide sequences of the VGAM928 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM928 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM928 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM928 are further de-

scribed hereinbelow with reference to Table 1.

[12958] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM928 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12959] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 929 (VGAM929) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12960] VGAM929 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM929 was detected is described hereinabove with reference to Figs. 2-8.

[12961] VGAM929 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM929 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12962] VGAM929 gene, herein designated VGAM GENE, encodes a VGAM929 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM929 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM929 precursor RNA is designated SEQ ID:24163, and is provided hereinbelow with reference to the sequence listing part.

[12963] VGAM929 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM929 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12964] An enzyme complex designated DICER COMPLEX, dices the VGAM929 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM929 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM929 RNA is designated SEQ ID:24164, and is provided hereinbelow with reference to the sequence listing part.

[12965] VGAM929 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12966] VGAM929 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM929 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM929 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12967] The complementary binding of VGAM929 RNA, herein designated VGAM RNA, to host target binding sites on VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM929 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12968] It is appreciated that VGAM929 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM929 host target genes. The mRNA of each one of this plurality of VGAM929 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM929 RNA, herein designated VGAM RNA, and which when bound by VGAM929 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM929 host target proteins.

[12969] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM929 gene, herein designated VGAM GENE, on one or more VGAM929 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12970] It is yet further appreciated that a function of VGAM929 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM929 correlate with, and may be deduced from, the identity of the host target genes which VGAM929 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12971] Nucleotide sequences of the VGAM929 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM929 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM929 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM929 are further described hereinbelow with reference to Table 1.

[12972] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM929 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12973] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 930 (VGAM930) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12974] VGAM930 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM930 was detected is described hereinabove with reference to Figs. 2-8.

[12975] VGAM930 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Odontoglossum ringspot virus. VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12976] VGAM930 gene, herein designated VGAM GENE, encodes a

VGAM930 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM930 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM930 precursor RNA is designated SEQ ID:24168, and is provided hereinbelow with reference to the sequence listing part.

[12977] VGAM930 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM930 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12978] An enzyme complex designated DICER COMPLEX, dices the VGAM930 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM930 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM930 RNA is designated SEQ ID:24169, and is provided hereinbelow with reference to the sequence listing part.

[12979] VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12980] VGAM930 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM930 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM930 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12981] The complementary binding of VGAM930 RNA, herein designated VGAM RNA, to host target binding sites on VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM930 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[12982] It is appreciated that VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM930 host target genes. The mRNA of each one of this plurality of VGAM930 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM930 RNA, herein designated VGAM RNA, and which when bound by VGAM930 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM930 host target proteins.

[12983] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM930 gene, herein designated VGAM GENE, on one or more VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12984] It is yet further appreciated that a function of VGAM930 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of viral infection by Odontoglossum ringspot virus. Specific functions, and accordingly utilities, of VGAM930 correlate with, and may be deduced from, the identity of the host target genes which VGAM930 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12985] Nucleotide sequences of the VGAM930 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM930 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM930 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM930 are further described hereinbelow with reference to Table 1.

[12986] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM930 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12987] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 931 (VGAM931) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12988] VGAM931 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM931 was detected is described hereinabove with reference to Figs. 2-8.

[12989] VGAM931 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM931 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12990] VGAM931 gene, herein designated VGAM GENE, encodes a VGAM931 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM931 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM931 precursor RNA is designated SEQ ID:24186, and is provided hereinbelow with reference to the sequence listing part.

[12991] VGAM931 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM931 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12992] An enzyme complex designated DICER COMPLEX, dices the VGAM931 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM931 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM931 RNA is designated SEQ ID:24187, and is provided hereinbelow with reference to the sequence listing part.

[12993] VGAM931 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[12994] VGAM931 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM931 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[12995] The complementary binding of VGAM931 RNA, herein designated VGAM RNA, to host target binding sites on VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM931 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12996] It is appreciated that VGAM931 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM931 host target genes. The mRNA of each one of this plurality of VGAM931 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM931 RNA, herein designated VGAM RNA, and which when bound by VGAM931 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM931 host target proteins.

[12997] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM931 gene, herein designated VGAM GENE, on one or more VGAM931 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[12998] It is yet further appreciated that a function of VGAM931 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of viral infection by Molluscum contagiosum virus. Specific functions, and accordingly utilities, of VGAM931 correlate with, and may be deduced from, the identity of the host target genes which VGAM931 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12999] Nucleotide sequences of the VGAM931 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM931 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM931 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM931 are further described hereinbelow with reference to Table 1.

[13000] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM931 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13001] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 932 (VGAM932) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13002] VGAM932 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM932 was detected is described hereinabove with reference to Figs. 2–8.

[13003] VGAM932 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM932 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13004] VGAM932 gene, herein designated VGAM GENE, encodes a VGAM932 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike



most ordinary genes, VGAM932 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM932 precursor RNA is designated SEQ ID:24211, and is provided hereinbelow with reference to the sequence listing part.

[13005] VGAM932 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM932 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13006] An enzyme complex designated DICER COMPLEX, dices the VGAM932 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM932 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM932 RNA is designated SEQ ID:24212, and is provided hereinbelow with reference to the sequence listing part.

[13007] VGAM932 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13008] VGAM932 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM932 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM932 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13009] The complementary binding of VGAM932 RNA, herein designated VGAM RNA, to host target binding sites on VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM932 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13010] It is appreciated that VGAM932 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM932 host target genes. The mRNA of each one of this plurality of VGAM932 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM932 RNA, herein designated VGAM RNA, and which when bound by VGAM932 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM932 host target proteins.

[13011] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM932 gene, herein designated VGAM GENE, on one or more VGAM932 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13012] It is yet further appreciated that a function of VGAM932 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM932 include diagnosis, prevention and treatment of viral infection by Molluscum contagiosum virus. Specific functions, and accordingly utilities, of VGAM932 correlate with, and may be deduced from, the identity of the host target genes which VGAM932 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13013] Nucleotide sequences of the VGAM932 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM932 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM932 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM932 are further described hereinbelow with reference to Table 1.

[13014] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM932 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13015] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 933 (VGAM933) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13016] VGAM933 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM933 was detected is described hereinabove with reference to Figs. 2–8.

[13017] VGAM933 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13018] VGAM933 gene, herein designated VGAM GENE, encodes a VGAM933 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM933 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM933 precursor RNA is designated SEQ ID:24296, and is provided hereinbelow with reference to the sequence listing part.

[13019] VGAM933 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM933 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13020] An enzyme complex designated DICER COMPLEX, dices the VGAM933 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM933 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM933 RNA is designated SEQ ID:24297, and is provided hereinbelow with reference to the sequence listing part.

[13021] VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13022] VGAM933 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM933 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13023] The complementary binding of VGAM933 RNA, herein designated VGAM RNA, to host target binding sites on VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM933 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13024] It is appreciated that VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM933 host target genes. The mRNA of each one of this plurality of VGAM933 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM933 RNA, herein designated VGAM RNA, and which when bound by VGAM933 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM933 host target proteins.

[13025] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM933 gene, herein designated VGAM GENE, on one or more VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[13026] It is yet further appreciated that a function of VGAM933 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM933 correlate with, and may be deduced from, the identity of the host target genes which VGAM933 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[13027] Nucleotide sequences of the VGAM933 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM933 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM933 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM933 are further described hereinbelow with reference to Table 1.

[13028] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM933 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13029] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 934 (VGAM934) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13030] VGAM934 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM934 was detected is described hereinabove with reference to Figs. 2–8.

[13031] VGAM934 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine foamy virus. VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13032] VGAM934 gene, herein designated VGAM GENE, encodes a VGAM934 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM934 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM934 precursor RNA is designated SEQ ID:24356, and is provided hereinbelow with reference to the sequence listing part.

[13033] VGAM934 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM934 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13034] An enzyme complex designated DICER COMPLEX, dices the VGAM934 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM934 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM934 RNA is designated SEQ ID:24357, and is provided hereinbelow with reference to the sequence listing part.

[13035] VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13036] VGAM934 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM934 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM934 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13037] The complementary binding of VGAM934 RNA, herein designated VGAM RNA, to host target binding sites on VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM934 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13038] It is appreciated that VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM934 host target genes. The mRNA of

each one of this plurality of VGAM934 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM934 RNA, herein designated VGAM RNA, and which when bound by VGAM934 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM934 host target proteins.

[13039] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM934 gene, herein designated VGAM GENE, on one or more VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[13040] It is yet further appreciated that a function of VGAM934 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM934 include diagnosis, prevention and treatment of viral infection by Equine foamy virus. Specific functions, and accordingly utilities, of VGAM934 correlate with, and may be deduced from, the identity of the host target genes which VGAM934 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13041] Nucleotide sequences of the VGAM934 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM934 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM934 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM934 are further described hereinbelow with reference to Table 1.

[13042] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM934 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[13043] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 935 (VGAM935) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13044] VGAM935 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM935 was detected is described hereinabove with reference to Figs. 2–8.

[13045] VGAM935 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine foamy virus. VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13046] VGAM935 gene, herein designated VGAM GENE, encodes a VGAM935 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM935 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM935 precursor RNA is designated SEQ ID:24382, and is provided hereinbelow with reference to the sequence listing part.

[13047] VGAM935 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM935 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13048] An enzyme complex designated DICER COMPLEX, dices the VGAM935 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM935 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM935 RNA is designated SEQ ID:24383, and

is provided hereinbelow with reference to the sequence listing part.

[13049] VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13050] VGAM935 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM935 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM935 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13051] The complementary binding of VGAM935 RNA, herein designated VGAM RNA, to host target binding sites on VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM935 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13052] It is appreciated that VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM935 host target genes. The mRNA of each one of this plurality of VGAM935 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM935 RNA, herein designated VGAM RNA, and which when bound by VGAM935 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM935 host target proteins.

[13053] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM935 gene, herein designated VGAM GENE, on one or more VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13054] It is yet further appreciated that a function of VGAM935 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM935 include diagnosis, prevention and treatment of viral infection by Equine foamy virus. Specific functions, and accordingly utilities, of VGAM935 correlate with, and may be deduced from, the identity of the host target genes which VGAM935 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13055] Nucleotide sequences of the VGAM935 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM935 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM935 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM935 are further described hereinbelow with reference to Table 1.

[13056] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM935 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13057] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 936 (VGAM936) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13058] VGAM936 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM936 was detected is described hereinabove with reference to Figs. 2–8.

[13059] VGAM936 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13060] VGAM936 gene, herein designated VGAM GENE, encodes a VGAM936 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM936 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM936 precursor RNA is



designated SEQ ID:24386, and is provided hereinbelow with reference to the sequence listing part.

[13061] VGAM936 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM936 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13062] An enzyme complex designated DICER COMPLEX, dices the VGAM936 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM936 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM936 RNA is designated SEQ ID:24387, and is provided hereinbelow with reference to the sequence

listing part.

[13063] VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13064] VGAM936 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM936 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM936 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13065] The complementary binding of VGAM936 RNA, herein designated VGAM RNA, to host target binding sites on VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM936 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13066] It is appreciated that VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM936 host target genes. The mRNA of each one of this plurality of VGAM936 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM936 RNA, herein designated VGAM RNA, and which when bound by VGAM936 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM936 host target proteins.

[13067] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM936 gene, herein designated VGAM GENE, on one or more VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13068] It is yet further appreciated that a function of VGAM936 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM936 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM936 correlate with, and may be deduced from, the identity of the host target genes which VGAM936 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13069] Nucleotide sequences of the VGAM936 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM936 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM936 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM936 are further described hereinbelow with reference to Table 1.

[13070] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM936 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13071] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 937 (VGAM937) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13072] VGAM937 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM937 was detected is described hereinabove with reference to Figs. 2–8.

[13073] VGAM937 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13074] VGAM937 gene, herein designated VGAM GENE, encodes a VGAM937 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM937 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM937 precursor RNA is designated SEQ ID:24400, and is provided hereinbelow

with reference to the sequence listing part.

[13075] VGAM937 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM937 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13076] An enzyme complex designated DICER COMPLEX, dices the VGAM937 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM937 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM937 RNA is designated SEQ ID:24401, and is provided hereinbelow with reference to the sequence listing part.

[13077] VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13078] VGAM937 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM937 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM937 RNA, herein designated



VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13079] The complementary binding of VGAM937 RNA, herein designated VGAM RNA, to host target binding sites on VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM937 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13080] It is appreciated that VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM937 host target genes. The mRNA of each one of this plurality of VGAM937 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM937 RNA, herein designated VGAM RNA, and which when bound by VGAM937 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM937 host target proteins.

[13081] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM937 gene, herein designated VGAM GENE, on one or more VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13082] It is yet further appreciated that a function of VGAM937 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM937 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM937 correlate with, and may be deduced from, the identity of the host target genes which VGAM937 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13083] Nucleotide sequences of the VGAM937 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM937 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM937 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM937 are further described hereinbelow with reference to Table 1.

[13084] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM937 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13085] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 938 (VGAM938) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13086] VGAM938 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM938 was detected is described hereinabove with reference to Figs. 2–8.

[13087] VGAM938 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM938 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13088] VGAM938 gene, herein designated VGAM GENE, encodes a VGAM938 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM938 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM938 precursor RNA is designated SEQ ID:24409, and is provided hereinbelow with reference to the sequence listing part.

[13089] VGAM938 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM938 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13090] An enzyme complex designated DICER COMPLEX, dices the VGAM938 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM938 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM938 RNA is designated SEQ ID:24410, and is provided hereinbelow with reference to the sequence listing part.

[13091] VGAM938 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13092] VGAM938 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM938 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM938 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13093] The complementary binding of VGAM938 RNA, herein designated VGAM RNA, to host target binding sites on VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM938 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13094] It is appreciated that VGAM938 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM938 host target genes. The mRNA of each one of this plurality of VGAM938 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM938 RNA, herein designated VGAM

RNA, and which when bound by VGAM938 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM938 host target proteins.

[13095] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM938 gene, herein designated VGAM GENE, on one or more VGAM938 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13096] It is yet further appreciated that a function of VGAM938 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM938 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM938 correlate with, and may be deduced from, the identity of the host target genes which VGAM938 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13097] Nucleotide sequences of the VGAM938 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM938 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM938 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM938 are further described hereinbelow with reference to Table 1.

[13098] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM938 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13099] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 939 (VGAM939) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13100] VGAM939 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM939 was detected is described hereinabove with reference to Figs. 2-8.

[13101] VGAM939 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13102] VGAM939 gene, herein designated VGAM GENE, encodes a VGAM939 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM939 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM939 precursor RNA is designated SEQ ID:24414, and is provided hereinbelow with reference to the sequence listing part.

[13103] VGAM939 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM939 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13104] An enzyme complex designated DICER COMPLEX, dices the VGAM939 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM939 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM939 RNA is designated SEQ ID:24415, and is provided hereinbelow with reference to the sequence listing part.

[13105] VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13106] VGAM939 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM939 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM939 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13107] The complementary binding of VGAM939 RNA, herein designated VGAM RNA, to host target binding sites on VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM939 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13108] It is appreciated that VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM939 host target genes. The mRNA of each one of this plurality of VGAM939 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM939 RNA, herein designated VGAM RNA, and which when bound by VGAM939 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM939 host target proteins.

[13109] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM939 gene, herein designated VGAM GENE, on one or more VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13110] It is yet further appreciated that a function of VGAM939 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM939 include diagnosis, prevention and

treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM939 correlate with, and may be deduced from, the identity of the host target genes which VGAM939 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [13111] Nucleotide sequences of the VGAM939 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM939 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM939 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM939 are further described hereinbelow with reference to Table 1.
- [13112] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM939 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [13113] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 940 (VGAM940) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13114] VGAM940 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM940 was detected is described hereinabove with reference to Figs. 2–8.

[13115] VGAM940 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 25. VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13116] VGAM940 gene, herein designated VGAM GENE, encodes a VGAM940 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM940 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM940 precursor RNA is designated SEQ ID:24435, and is provided hereinbelow with reference to the sequence listing part.

[13117] VGAM940 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM940 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13118] An enzyme complex designated DICER COMPLEX, dices the VGAM940 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM940 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM940 RNA is designated SEQ ID:24436, and is provided hereinbelow with reference to the sequence listing part.

[13119] VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM940 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13120] VGAM940 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM940 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13121] The complementary binding of VGAM940 RNA, herein designated VGAM RNA, to host target binding sites on VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM940 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13122] It is appreciated that VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM940 host target genes. The mRNA of each one of this plurality of VGAM940 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM940 RNA, herein designated VGAM RNA, and which when bound by VGAM940 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM940 host target proteins.

[13123] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM940 gene, herein designated VGAM GENE, on one or more VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13124] It is yet further appreciated that a function of VGAM940 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type

25. Specific functions, and accordingly utilities, of VGAM940 correlate with, and may be deduced from, the identity of the host target genes which VGAM940 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13125] Nucleotide sequences of the VGAM940 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM940 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM940 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM940 are further described hereinbelow with reference to Table 1.

[13126] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM940 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13127] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 941 (VGAM941) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[13128] VGAM941 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM941 was detected is described hereinabove with reference to Figs. 2–8.

[13129] VGAM941 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 25. VGAM941 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13130] VGAM941 gene, herein designated VGAM GENE, encodes a VGAM941 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM941 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM941 precursor RNA is designated SEQ ID:25019, and is provided hereinbelow with reference to the sequence listing part.

[13131] VGAM941 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM941 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13132] An enzyme complex designated DICER COMPLEX, dices the VGAM941 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM941 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM941 RNA is designated SEQ ID:25020, and is provided hereinbelow with reference to the sequence listing part.

[13133] VGAM941 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM941 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13134] VGAM941 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM941 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13135] The complementary binding of VGAM941 RNA, herein designated VGAM RNA, to host target binding sites on VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM941 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13136] It is appreciated that VGAM941 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM941 host target genes. The mRNA of each one of this plurality of VGAM941 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM941 RNA, herein designated VGAM RNA, and which when bound by VGAM941 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM941 host target proteins.

[13137] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM941 gene, herein designated VGAM GENE, on one or more VGAM941 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13138] It is yet further appreciated that a function of VGAM941 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 25. Specific functions, and accordingly utilities, of

VGAM941 correlate with, and may be deduced from, the identity of the host target genes which VGAM941 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13139] Nucleotide sequences of the VGAM941 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM941 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM941 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM941 are further described hereinbelow with reference to Table 1.

[13140] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM941 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13141] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 942 (VGAM942) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[13142] VGAM942 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM942 was detected is described hereinabove with reference to Figs. 2–8.

[13143] VGAM942 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13144] VGAM942 gene, herein designated VGAM GENE, encodes a VGAM942 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM942 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM942 precursor RNA is designated SEQ ID:25049, and is provided hereinbelow with reference to the sequence listing part.

[13145] VGAM942 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM942 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13146] An enzyme complex designated DICER COMPLEX, dices the VGAM942 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM942 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM942 RNA is designated SEQ ID:25050, and is provided hereinbelow with reference to the sequence listing part.

[13147] VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13148] VGAM942 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM942 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13149] The complementary binding of VGAM942 RNA, herein designated VGAM RNA, to host target binding sites on VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM942 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13150] It is appreciated that VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM942 host target genes. The mRNA of each one of this plurality of VGAM942 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM942 RNA, herein designated VGAM RNA, and which when bound by VGAM942 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM942 host target proteins.

[13151] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM942 gene, herein designated VGAM GENE, on one or more VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13152] It is yet further appreciated that a function of VGAM942 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM942 correlate with, and may be deduced from, the identity of



the host target genes which VGAM942 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13153] Nucleotide sequences of the VGAM942 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM942 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM942 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM942 are further described hereinbelow with reference to Table 1.

[13154] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM942 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13155] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 943 (VGAM943) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13156] VGAM943 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM943 was detected is described hereinabove with reference to Figs. 2–8.

[13157] VGAM943 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13158] VGAM943 gene, herein designated VGAM GENE, encodes a VGAM943 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM943 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM943 precursor RNA is designated SEQ ID:25077, and is provided hereinbelow with reference to the sequence listing part.

[13159] VGAM943 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM943 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13160] An enzyme complex designated DICER COMPLEX, dices the VGAM943 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM943 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM943 RNA is designated SEQ ID:25078, and is provided hereinbelow with reference to the sequence listing part.

[13161] VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13162] VGAM943 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM943 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13163] The complementary binding of VGAM943 RNA, herein designated VGAM RNA, to host target binding sites on VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM943 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13164] It is appreciated that VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM943 host target genes. The mRNA of each one of this plurality of VGAM943 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM943 RNA, herein designated VGAM RNA, and which when bound by VGAM943 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM943 host target proteins.

[13165] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM943 gene, herein designated VGAM GENE, on one or more VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13166] It is yet further appreciated that a function of VGAM943 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM943 correlate with, and may be deduced from, the identity of the host target genes which VGAM943 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[13167] Nucleotide sequences of the VGAM943 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM943 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM943 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM943 are further described hereinbelow with reference to Table 1.

[13168] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM943 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13169] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 944 (VGAM944) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13170] VGAM944 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM944 was detected is described hereinabove with reference to Figs. 2–8.

[13171] VGAM944 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13172] VGAM944 gene, herein designated VGAM GENE, encodes a VGAM944 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM944 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM944 precursor RNA is designated SEQ ID:25098, and is provided hereinbelow with reference to the sequence listing part.

[13173] VGAM944 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM944 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the



fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13174] An enzyme complex designated DICER COMPLEX, dices the VGAM944 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM944 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM944 RNA is designated SEQ ID:25099, and is provided hereinbelow with reference to the sequence listing part.

[13175] VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13176] VGAM944 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM944 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM944 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3'UTR and 5'UTR regions.

[13177] The complementary binding of VGAM944 RNA, herein designated VGAM RNA, to host target binding sites on VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM944 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13178] It is appreciated that VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM944 host target genes. The mRNA of each one of this plurality of VGAM944 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM944 RNA, herein designated VGAM RNA, and which when bound by VGAM944 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM944 host target proteins.

[13179] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM944 gene, herein designated VGAM GENE, on one or more VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13180] It is yet further appreciated that a function of VGAM944 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM944 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM944 correlate with, and may be deduced from, the identity of the host target genes which VGAM944 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[13181] Nucleotide sequences of the VGAM944 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM944 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM944 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM944 are further described hereinbelow with reference to Table 1.

[13182] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM944 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13183] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 945 (VGAM945) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13184] VGAM945 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM945 was detected is described hereinabove with reference to Figs. 2–8.

[13185] VGAM945 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM945 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13186] VGAM945 gene, herein designated VGAM GENE, encodes a VGAM945 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM945 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM945 precursor RNA is designated SEQ ID:25107, and is provided hereinbelow with reference to the sequence listing part.

[13187] VGAM945 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM945 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13188] An enzyme complex designated DICER COMPLEX, dices the VGAM945 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM945 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM945 RNA is designated SEQ ID:25108, and is provided hereinbelow with reference to the sequence listing part.

[13189] VGAM945 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[13190] VGAM945 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM945 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[13191] The complementary binding of VGAM945 RNA, herein designated VGAM RNA, to host target binding sites on VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM945 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13192] It is appreciated that VGAM945 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM945 host target genes. The mRNA of each one of this plurality of VGAM945 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM945 RNA, herein designated VGAM RNA, and which when bound by VGAM945 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM945 host target proteins.

[13193] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM945 gene, herein designated VGAM GENE, on one or

more VGAM945 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13194] It is yet further appreciated that a function of VGAM945 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM945 correlate with, and may be deduced from, the identity of the host target genes which VGAM945 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13195] Nucleotide sequences of the VGAM945 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM945 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM945 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM945 are further described hereinbelow with reference to Table 1.

[13196] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM945 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13197] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 946 (VGAM946) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13198] VGAM946 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM946 was detected is described

hereinabove with reference to Figs. 2–8.

[13199] VGAM946 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM946 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13200] VGAM946 gene, herein designated VGAM GENE, encodes a VGAM946 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM946 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM946 precursor RNA is designated SEQ ID:25115, and is provided hereinbelow with reference to the sequence listing part.

[13201] VGAM946 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM946 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13202] An enzyme complex designated DICER COMPLEX, dices the VGAM946 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM946 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM946 RNA is designated SEQ ID:25116, and is provided hereinbelow with reference to the sequence listing part.

[13203] VGAM946 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13204] VGAM946 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM946 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM946 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13205] The complementary binding of VGAM946 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM946 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13206] It is appreciated that VGAM946 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM946 host target genes. The mRNA of each one of this plurality of VGAM946 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM946 RNA, herein designated VGAM RNA, and which when bound by VGAM946 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM946 host target proteins.

[13207] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM946 gene, herein designated VGAM GENE, on one or more VGAM946 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13208] It is yet further appreciated that a function of VGAM946 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM946 correlate with, and may be deduced from, the identity of the host target genes which VGAM946 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13209] Nucleotide sequences of the VGAM946 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM946 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM946 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM946 are further described hereinbelow with reference to Table 1.

[13210] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM946 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13211] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 947 (VGAM947) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13212] VGAM947 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM947 was detected is described hereinabove with reference to Figs. 2-8.

[13213] VGAM947 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM947 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13214] VGAM947 gene, herein designated VGAM GENE, encodes a VGAM947 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM947 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM947 precursor RNA is designated SEQ ID:25126, and is provided hereinbelow with reference to the sequence listing part.

[13215] VGAM947 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM947 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[13216] An enzyme complex designated DICER COMPLEX, dices the VGAM947 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM947 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM947 RNA is designated SEQ ID:25127, and is provided hereinbelow with reference to the sequence listing part.

[13217] VGAM947 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13218] VGAM947 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM947 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM947 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13219] The complementary binding of VGAM947 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM947 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13220] It is appreciated that VGAM947 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM947 host target genes. The mRNA of each one of this plurality of VGAM947 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM947 RNA, herein designated VGAM RNA, and which when bound by VGAM947 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM947 host target proteins.

[13221] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM947 gene, herein designated VGAM GENE, on one or more VGAM947 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13222] It is yet further appreciated that a function of VGAM947 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM947 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM947 correlate with, and may be deduced from, the identity of the host target genes which VGAM947 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13223] Nucleotide sequences of the VGAM947 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM947 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM947 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM947 are further described hereinbelow with reference to Table 1.

[13224] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM947 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13225] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 948 (VGAM948) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13226] VGAM948 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM948 was detected is described hereinabove with reference to Figs. 2-8.

[13227] VGAM948 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Sheep astrovirus.

VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13228] VGAM948 gene, herein designated VGAM GENE, encodes a VGAM948 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM948 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM948 precursor RNA is designated SEQ ID:25133, and is provided hereinbelow with reference to the sequence listing part.

[13229] VGAM948 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM948 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[13230] An enzyme complex designated DICER COMPLEX, dices the VGAM948 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM948 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM948 RNA is designated SEQ ID:25134, and is provided hereinbelow with reference to the sequence listing part.

[13231] VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13232] VGAM948 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM948 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM948 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13233] The complementary binding of VGAM948 RNA, herein designated VGAM RNA, to host target binding sites on VGAM948 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM948 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13234] It is appreciated that VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM948 host target genes. The mRNA of each one of this plurality of VGAM948 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM948 RNA, herein designated VGAM RNA, and which when bound by VGAM948 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM948 host target proteins.

[13235] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM948 gene, herein designated VGAM GENE, on one or more VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13236] It is yet further appreciated that a function of VGAM948 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM948 include diagnosis, prevention and treatment of viral infection by Sheep astrovirus. Specific functions, and accordingly utilities, of VGAM948 correlate with, and may be deduced from, the identity of the host target genes which VGAM948 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13237] Nucleotide sequences of the VGAM948 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM948 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM948 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM948 are further described hereinbelow with reference to Table 1.

[13238] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM948 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13239] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 949 (VGAM949) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13240] VGAM949 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM949 was detected is described hereinabove with reference to Figs. 2-8.

[13241] VGAM949 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Amsacta moorei* ento-

mopoxvirus. VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13242] VGAM949 gene, herein designated VGAM GENE, encodes a VGAM949 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM949 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM949 precursor RNA is designated SEQ ID:25185, and is provided hereinbelow with reference to the sequence listing part.

[13243] VGAM949 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM949 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13244] An enzyme complex designated DICER COMPLEX, dices

the VGAM949 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM949 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM949 RNA is designated SEQ ID:25186, and is provided hereinbelow with reference to the sequence listing part.

[13245] VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13246] VGAM949 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM949 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM949 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13247] The complementary binding of VGAM949 RNA, herein designated VGAM RNA, to host target binding sites on VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and



BINDING SITE III, inhibits translation of VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM949 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13248] It is appreciated that VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM949 host target genes. The mRNA of each one of this plurality of VGAM949 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM949 RNA, herein designated VGAM RNA, and which when bound by VGAM949 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM949 host target proteins.

[13249] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM949 gene, herein designated VGAM GENE, on one or more VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13250] It is yet further appreciated that a function of VGAM949 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM949 correlate with, and may be deduced from, the identity of the host target genes which VGAM949 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13251] Nucleotide sequences of the VGAM949 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM949 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM949 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM949 are further described hereinbelow with reference to Table 1.

[13252] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM949 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13253] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 950 (VGAM950) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13254] VGAM950 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM950 was detected is described hereinabove with reference to Figs. 2-8.

[13255] VGAM950 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus. VGAM950 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[13256] VGAM950 gene, herein designated VGAM GENE, encodes a VGAM950 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM950 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM950 precursor RNA is designated SEQ ID:25197, and is provided hereinbelow with reference to the sequence listing part.

[13257] VGAM950 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM950 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13258] An enzyme complex designated DICER COMPLEX, dices the VGAM950 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM950 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM950 RNA is designated SEQ ID:25198, and is provided hereinbelow with reference to the sequence listing part.

[13259] VGAM950 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13260] VGAM950 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM950 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM950 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13261] The complementary binding of VGAM950 RNA, herein designated VGAM RNA, to host target binding sites on VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM950 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM950 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13262] It is appreciated that VGAM950 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM950 host target genes. The mRNA of each one of this plurality of VGAM950 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM950 RNA, herein designated VGAM RNA, and which when bound by VGAM950 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM950 host target proteins.

[13263] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM950 gene, herein designated VGAM GENE, on one or more VGAM950 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13264] It is yet further appreciated that a function of VGAM950 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM950 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM950 correlate with, and may be deduced from, the identity of the host target genes which VGAM950 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13265] Nucleotide sequences of the VGAM950 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM950 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM950 folded precursor RNA, herein designated VGAM



FOLDED PRECURSOR RNA, of VGAM950 are further described hereinbelow with reference to Table 1.

[13266] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM950 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13267] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 951 (VGAM951) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13268] VGAM951 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM951 was detected is described hereinabove with reference to Figs. 2-8.

[13269] VGAM951 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus. VGAM951 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13270] VGAM951 gene, herein designated VGAM GENE, encodes a

VGAM951 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM951 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM951 precursor RNA is designated SEQ ID:25207, and is provided hereinbelow with reference to the sequence listing part.

[13271] VGAM951 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM951 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13272] An enzyme complex designated DICER COMPLEX, dices the VGAM951 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM951 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM951 RNA is designated SEQ ID:25208, and is provided hereinbelow with reference to the sequence listing part.

[13273] VGAM951 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13274] VGAM951 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM951 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM951 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13275] The complementary binding of VGAM951 RNA, herein designated VGAM RNA, to host target binding sites on VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM951 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[13276] It is appreciated that VGAM951 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM951 host target genes. The mRNA of each one of this plurality of VGAM951 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM951 RNA, herein designated VGAM RNA, and which when bound by VGAM951 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM951 host target proteins.

[13277] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM951 gene, herein designated VGAM GENE, on one or more VGAM951 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13278] It is yet further appreciated that a function of VGAM951 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM951 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM951 correlate with, and may be deduced from, the identity of the host target genes which VGAM951 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13279] Nucleotide sequences of the VGAM951 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM951 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM951 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM951 are further described hereinbelow with reference to Table 1.

[13280] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM951 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13281] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 952 (VGAM952) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13282] VGAM952 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM952 was detected is described hereinabove with reference to Figs. 2-8.

[13283] VGAM952 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13284] VGAM952 gene, herein designated VGAM GENE, encodes a VGAM952 precursor RNA, herein designated VGAM PRE-



CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM952 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM952 precursor RNA is designated SEQ ID:25234, and is provided hereinbelow with reference to the sequence listing part.

[13285] VGAM952 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM952 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13286] An enzyme complex designated DICER COMPLEX, dices the VGAM952 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM952 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM952 RNA is designated SEQ ID:25235, and is provided hereinbelow with reference to the sequence listing part.

[13287] VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13288] VGAM952 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM952 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13289] The complementary binding of VGAM952 RNA, herein designated VGAM RNA, to host target binding sites on VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM952 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13290] It is appreciated that VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM952 host target genes. The mRNA of each one of this plurality of VGAM952 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM952 RNA, herein designated VGAM RNA, and which when bound by VGAM952 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM952 host target proteins.

[13291] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM952 gene, herein designated VGAM GENE, on one or more VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13292] It is yet further appreciated that a function of VGAM952 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM952 correlate with, and may be deduced from, the identity of the host target genes which VGAM952 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13293] Nucleotide sequences of the VGAM952 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM952 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM952 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM952 are further described hereinbelow with reference to Table 1.

[13294] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM952 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13295] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 953 (VGAM953) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13296] VGAM953 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM953 was detected is described hereinabove with reference to Figs. 2–8.

[13297] VGAM953 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fujinami sarcoma virus. VGAM953 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13298] VGAM953 gene, herein designated VGAM GENE, encodes a VGAM953 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM953 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM953 precursor RNA is designated SEQ ID:25242, and is provided hereinbelow with reference to the sequence listing part.

[13299] VGAM953 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM953 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13300] An enzyme complex designated DICER COMPLEX, dices the VGAM953 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM953 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM953 RNA is designated SEQ ID:25243, and is provided hereinbelow with reference to the sequence listing part.

[13301] VGAM953 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13302] VGAM953 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM953 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13303] The complementary binding of VGAM953 RNA, herein designated VGAM RNA, to host target binding sites on VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM953 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13304] It is appreciated that VGAM953 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM953 host target genes. The mRNA of each one of this plurality of VGAM953 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM953 RNA, herein designated VGAM RNA, and which when bound by VGAM953 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM953 host target proteins.

[13305] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM953 gene, herein designated VGAM GENE, on one or more VGAM953 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13306] It is yet further appreciated that a function of VGAM953 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of viral infection by Fujinami sarcoma virus. Specific functions, and accordingly utilities, of VGAM953 correlate with, and may be deduced from, the identity of the host target genes which VGAM953 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13307] Nucleotide sequences of the VGAM953 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM953 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM953 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM953 are further described hereinbelow with reference to Table 1.

[13308] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM953 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13309] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 954 (VGAM954) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13310] VGAM954 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM954 was detected is described hereinabove with reference to Figs. 2–8.

[13311] VGAM954 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fujinami sarcoma virus. VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13312] VGAM954 gene, herein designated VGAM GENE, encodes a VGAM954 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM954 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM954 precursor RNA is designated SEQ ID:25246, and is provided hereinbelow with reference to the sequence listing part.

[13313] VGAM954 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM954 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13314] An enzyme complex designated DICER COMPLEX, dices the VGAM954 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM954 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 75%) nucleotide sequence of VGAM954 RNA is designated SEQ ID:25247, and is provided hereinbelow with reference to the sequence listing part.

[13315] VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13316] VGAM954 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM954 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13317] The complementary binding of VGAM954 RNA, herein designated VGAM RNA, to host target binding sites on VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM954 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13318] It is appreciated that VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM954 host target genes. The mRNA of each one of this plurality of VGAM954 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM954 RNA, herein designated VGAM RNA, and which when bound by VGAM954 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM954 host target proteins.

[13319] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM954 gene, herein designated VGAM GENE, on one or more VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[13320] It is yet further appreciated that a function of VGAM954 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of viral infection by Fujinami sarcoma virus. Specific functions, and accordingly utilities, of VGAM954 correlate with, and may be deduced from, the identity of the host target genes which VGAM954 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13321] Nucleotide sequences of the VGAM954 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM954 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM954 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM954 are further described hereinbelow with reference to Table 1.

[13322] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM954 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13323] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 955 (VGAM955) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13324] VGAM955 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM955 was detected is described hereinabove with reference to Figs. 2–8.

[13325] VGAM955 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM955 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13326] VGAM955 gene, herein designated VGAM GENE, encodes a VGAM955 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM955 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM955 precursor RNA is designated SEQ ID:25263, and is provided hereinbelow with reference to the sequence listing part.

[13327] VGAM955 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM955 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13328] An enzyme complex designated DICER COMPLEX, dices the VGAM955 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM955 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM955 RNA is designated SEQ ID:25264, and is provided hereinbelow with reference to the sequence listing part.

[13329] VGAM955 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13330] VGAM955 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM955 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13331] The complementary binding of VGAM955 RNA, herein designated VGAM RNA, to host target binding sites on VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM955 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13332] It is appreciated that VGAM955 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM955 host target genes. The mRNA of

each one of this plurality of VGAM955 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM955 RNA, herein designated VGAM RNA, and which when bound by VGAM955 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM955 host target proteins.

[13333] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM955 gene, herein designated VGAM GENE, on one or more VGAM955 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[13334] It is yet further appreciated that a function of VGAM955 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM955 correlate with, and may be deduced from, the identity of the host target genes which VGAM955 binds and inhibits, and the function of these host target genes, as elaborated herein—below.

[13335] Nucleotide sequences of the VGAM955 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM955 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM955 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM955 are further described hereinbelow with reference to Table 1.

[13336] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM955 RNA, herein designated VGAM RNA, are de—

scribed hereinbelow with reference to Table 2.

[13337] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 956 (VGAM956) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13338] VGAM956 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM956 was detected is described hereinabove with reference to Figs. 2–8.

[13339] VGAM956 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13340] VGAM956 gene, herein designated VGAM GENE, encodes a VGAM956 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM956 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar



to the nucleotide sequence of VGAM956 precursor RNA is designated SEQ ID:25279, and is provided hereinbelow with reference to the sequence listing part.

[13341] VGAM956 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM956 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13342] An enzyme complex designated DICER COMPLEX, dices the VGAM956 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM956 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM956 RNA is designated SEQ ID:25280, and

is provided hereinbelow with reference to the sequence listing part.

[13343] VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13344] VGAM956 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM956 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM956 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13345] The complementary binding of VGAM956 RNA, herein designated VGAM RNA, to host target binding sites on VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM956 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13346] It is appreciated that VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM956 host target genes. The mRNA of each one of this plurality of VGAM956 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM956 RNA, herein designated VGAM RNA, and which when bound by VGAM956 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM956 host target proteins.

[13347] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM956 gene, herein designated VGAM GENE, on one or more VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13348] It is yet further appreciated that a function of VGAM956 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM956 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM956 correlate with, and may be deduced from, the identity of the host target genes which VGAM956 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13349] Nucleotide sequences of the VGAM956 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM956 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM956 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM956 are further described hereinbelow with reference to Table 1.

[13350] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM956 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13351] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 957 (VGAM957) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13352] VGAM957 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM957 was detected is described hereinabove with reference to Figs. 2–8.

[13353] VGAM957 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM957 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13354] VGAM957 gene, herein designated VGAM GENE, encodes a VGAM957 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM957 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM957 precursor RNA is

designated SEQ ID:25299, and is provided hereinbelow with reference to the sequence listing part.

[13355] VGAM957 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM957 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13356] An enzyme complex designated DICER COMPLEX, dices the VGAM957 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM957 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM957 RNA is designated SEQ ID:25300, and is provided hereinbelow with reference to the sequence

listing part.

[13357] VGAM957 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13358] VGAM957 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM957 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13359] The complementary binding of VGAM957 RNA, herein designated VGAM RNA, to host target binding sites on VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM957 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13360] It is appreciated that VGAM957 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM957 host target genes. The mRNA of each one of this plurality of VGAM957 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM957 RNA, herein designated VGAM RNA, and which when bound by VGAM957 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM957 host target proteins.

[13361] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM957 gene, herein designated VGAM GENE, on one or more VGAM957 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13362] It is yet further appreciated that a function of VGAM957 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM957 correlate with, and may be deduced from, the identity of the host target genes which VGAM957 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13363] Nucleotide sequences of the VGAM957 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM957 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM957 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM957 are further described hereinbelow with reference to Table 1.

[13364] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM957 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13365] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 958 (VGAM958) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13366] VGAM958 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM958 was detected is described hereinabove with reference to Figs. 2–8.

[13367] VGAM958 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13368] VGAM958 gene, herein designated VGAM GENE, encodes a VGAM958 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM958 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM958 precursor RNA is designated SEQ ID:25304, and is provided hereinbelow

with reference to the sequence listing part.

[13369] VGAM958 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM958 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13370] An enzyme complex designated DICER COMPLEX, dices the VGAM958 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM958 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM958 RNA is designated SEQ ID:25305, and is provided hereinbelow with reference to the sequence listing part.

[13371] VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13372] VGAM958 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM958 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13373] The complementary binding of VGAM958 RNA, herein designated VGAM RNA, to host target binding sites on VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM958 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13374] It is appreciated that VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM958 host target genes. The mRNA of each one of this plurality of VGAM958 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM958 RNA, herein designated VGAM RNA, and which when bound by VGAM958 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM958 host target proteins.

[13375] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM958 gene, herein designated VGAM GENE, on one or more VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13376] It is yet further appreciated that a function of VGAM958 is inhibition of expression of host target genes, as part of a



novel viral mechanism of attacking a host. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM958 correlate with, and may be deduced from, the identity of the host target genes which VGAM958 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13377] Nucleotide sequences of the VGAM958 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM958 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM958 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM958 are further described hereinbelow with reference to Table 1.

[13378] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM958 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13379] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 959 (VGAM959) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13380] VGAM959 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM959 was detected is described hereinabove with reference to Figs. 2–8.

[13381] VGAM959 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM959 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13382] VGAM959 gene, herein designated VGAM GENE, encodes a VGAM959 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM959 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM959 precursor RNA is designated SEQ ID:25383, and is provided hereinbelow with reference to the sequence listing part.

[13383] VGAM959 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM959 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13384] An enzyme complex designated DICER COMPLEX, dices the VGAM959 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM959 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM959 RNA is designated SEQ ID:25384, and is provided hereinbelow with reference to the sequence listing part.

[13385] VGAM959 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13386] VGAM959 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM959 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM959 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13387] The complementary binding of VGAM959 RNA, herein designated VGAM RNA, to host target binding sites on VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM959 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13388] It is appreciated that VGAM959 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM959 host target genes. The mRNA of each one of this plurality of VGAM959 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM959 RNA, herein designated VGAM

RNA, and which when bound by VGAM959 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM959 host target proteins.

[13389] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM959 gene, herein designated VGAM GENE, on one or more VGAM959 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13390] It is yet further appreciated that a function of VGAM959 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM959 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM959 correlate with, and may be deduced from, the identity of the host target genes which VGAM959 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13391] Nucleotide sequences of the VGAM959 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM959 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM959 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM959 are further described hereinbelow with reference to Table 1.

[13392] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM959 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13393] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 960 (VGAM960) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13394] VGAM960 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM960 was detected is described hereinabove with reference to Figs. 2–8.

[13395] VGAM960 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13396] VGAM960 gene, herein designated VGAM GENE, encodes a VGAM960 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM960 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM960 precursor RNA is designated SEQ ID:25386, and is provided hereinbelow with reference to the sequence listing part.

[13397] VGAM960 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM960 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13398] An enzyme complex designated DICER COMPLEX, dices the VGAM960 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM960 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM960 RNA is designated SEQ ID:25387, and is provided hereinbelow with reference to the sequence listing part.

[13399] VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13400] VGAM960 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM960 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM960 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM960 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13401] The complementary binding of VGAM960 RNA, herein designated VGAM RNA, to host target binding sites on VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM960 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13402] It is appreciated that VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM960 host target genes. The mRNA of each one of this plurality of VGAM960 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM960 RNA, herein designated VGAM RNA, and which when bound by VGAM960 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM960 host target proteins.

[13403] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM960 gene, herein designated VGAM GENE, on one or more VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13404] It is yet further appreciated that a function of VGAM960 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM960 include diagnosis, prevention and

treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM960 correlate with, and may be deduced from, the identity of the host target genes which VGAM960 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13405] Nucleotide sequences of the VGAM960 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM960 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM960 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM960 are further described hereinbelow with reference to Table 1.

[13406] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM960 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13407] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 961 (VGAM961) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13408] VGAM961 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM961 was detected is described hereinabove with reference to Figs. 2–8.

[13409] VGAM961 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13410] VGAM961 gene, herein designated VGAM GENE, encodes a VGAM961 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM961 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM961 precursor RNA is designated SEQ ID:25416, and is provided hereinbelow with reference to the sequence listing part.

[13411] VGAM961 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM961 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13412] An enzyme complex designated DICER COMPLEX, dices the VGAM961 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM961 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM961 RNA is designated SEQ ID:25417, and is provided hereinbelow with reference to the sequence listing part.

[13413] VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM961 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13414] VGAM961 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM961 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM961 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13415] The complementary binding of VGAM961 RNA, herein designated VGAM RNA, to host target binding sites on VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM961 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13416] It is appreciated that VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM961 host target genes. The mRNA of each one of this plurality of VGAM961 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM961 RNA, herein designated VGAM RNA, and which when bound by VGAM961 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM961 host target proteins.

[13417] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM961 gene, herein designated VGAM GENE, on one or more VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13418] It is yet further appreciated that a function of VGAM961 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM961 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Spe-

cific functions, and accordingly utilities, of VGAM961 correlate with, and may be deduced from, the identity of the host target genes which VGAM961 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13419] Nucleotide sequences of the VGAM961 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM961 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM961 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM961 are further described hereinbelow with reference to Table 1.

[13420] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM961 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13421] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 962 (VGAM962) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[13422] VGAM962 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM962 was detected is described hereinabove with reference to Figs. 2–8.

[13423] VGAM962 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM962 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13424] VGAM962 gene, herein designated VGAM GENE, encodes a VGAM962 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM962 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM962 precursor RNA is designated SEQ ID:25436, and is provided hereinbelow with reference to the sequence listing part.

[13425] VGAM962 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM962 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13426] An enzyme complex designated DICER COMPLEX, dices the VGAM962 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM962 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM962 RNA is designated SEQ ID:25437, and is provided hereinbelow with reference to the sequence listing part.

[13427] VGAM962 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM962 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13428] VGAM962 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM962 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM962 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13429] The complementary binding of VGAM962 RNA, herein designated VGAM RNA, to host target binding sites on VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM962 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13430] It is appreciated that VGAM962 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM962 host target genes. The mRNA of each one of this plurality of VGAM962 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM962 RNA, herein designated VGAM RNA, and which when bound by VGAM962 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM962 host target proteins.

[13431] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM962 gene, herein designated VGAM GENE, on one or more VGAM962 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13432] It is yet further appreciated that a function of VGAM962 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM962 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM962 cor-



relate with, and may be deduced from, the identity of the host target genes which VGAM962 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13433] Nucleotide sequences of the VGAM962 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM962 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM962 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM962 are further described hereinbelow with reference to Table 1.

[13434] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM962 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13435] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 963 (VGAM963) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[13436] VGAM963 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM963 was detected is described hereinabove with reference to Figs. 2–8.

[13437] VGAM963 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13438] VGAM963 gene, herein designated VGAM GENE, encodes a VGAM963 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM963 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM963 precursor RNA is designated SEQ ID:25458, and is provided hereinbelow with reference to the sequence listing part.

[13439] VGAM963 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM963 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13440] An enzyme complex designated DICER COMPLEX, dices the VGAM963 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM963 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM963 RNA is designated SEQ ID:25459, and is provided hereinbelow with reference to the sequence listing part.

[13441] VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13442] VGAM963 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM963 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM963 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13443] The complementary binding of VGAM963 RNA, herein designated VGAM RNA, to host target binding sites on VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM963 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13444] It is appreciated that VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM963 host target genes. The mRNA of each one of this plurality of VGAM963 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM963 RNA, herein designated VGAM RNA, and which when bound by VGAM963 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM963 host target proteins.

[13445] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM963 gene, herein designated VGAM GENE, on one or more VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13446] It is yet further appreciated that a function of VGAM963 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM963 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM963 correlate with, and may be deduced from,

the identity of the host target genes which VGAM963 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13447] Nucleotide sequences of the VGAM963 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM963 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM963 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM963 are further described hereinbelow with reference to Table 1.

[13448] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM963 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13449] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 964 (VGAM964) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13450] VGAM964 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM964 was detected is described hereinabove with reference to Figs. 2–8.

[13451] VGAM964 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13452] VGAM964 gene, herein designated VGAM GENE, encodes a VGAM964 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM964 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM964 precursor RNA is designated SEQ ID:25489, and is provided hereinbelow with reference to the sequence listing part.

[13453] VGAM964 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM964 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13454] An enzyme complex designated DICER COMPLEX, dices the VGAM964 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM964 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM964 RNA is designated SEQ ID:25490, and is provided hereinbelow with reference to the sequence listing part.

[13455] VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13456] VGAM964 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM964 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13457] The complementary binding of VGAM964 RNA, herein designated VGAM RNA, to host target binding sites on VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM964 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13458] It is appreciated that VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM964 host target genes. The mRNA of each one of this plurality of VGAM964 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM964 RNA, herein designated VGAM RNA, and which when bound by VGAM964 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM964 host target proteins.

[13459] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM964 gene, herein designated VGAM GENE, on one or more VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13460] It is yet further appreciated that a function of VGAM964 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM964 correlate with, and may be deduced from, the identity of the host target genes which VGAM964

binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13461] Nucleotide sequences of the VGAM964 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM964 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM964 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM964 are further described hereinbelow with reference to Table 1.

[13462] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM964 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13463] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 965 (VGAM965) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13464] VGAM965 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM965 was detected is described hereinabove with reference to Figs. 2–8.

[13465] VGAM965 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Citrus tristeza virus. VGAM965 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13466] VGAM965 gene, herein designated VGAM GENE, encodes a VGAM965 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM965 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM965 precursor RNA is designated SEQ ID:25495, and is provided hereinbelow with reference to the sequence listing part.

[13467] VGAM965 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM965 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13468] An enzyme complex designated DICER COMPLEX, dices the VGAM965 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM965 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM965 RNA is designated SEQ ID:25496, and is provided hereinbelow with reference to the sequence listing part.

[13469] VGAM965 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-

translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13470] VGAM965 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM965 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM965 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[13471] The complementary binding of VGAM965 RNA, herein designated VGAM RNA, to host target binding sites on VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM965 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13472] It is appreciated that VGAM965 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM965 host target genes. The mRNA of each one of this plurality of VGAM965 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM965 RNA, herein designated VGAM RNA, and which when bound by VGAM965 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM965 host target proteins.

[13473] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM965 gene, herein designated VGAM GENE, on one or more VGAM965 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13474] It is yet further appreciated that a function of VGAM965 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM965 include diagnosis, prevention and treatment of viral infection by Citrus tristeza virus. Specific functions, and accordingly utilities, of VGAM965 correlate with, and may be deduced from, the identity of the host target genes which VGAM965 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[13475] Nucleotide sequences of the VGAM965 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM965 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM965 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM965 are further described hereinbelow with reference to Table 1.

[13476] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM965 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13477] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 966 (VGAM966) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13478] VGAM966 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM966 was detected is described hereinabove with reference to Figs. 2–8.

[13479] VGAM966 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13480] VGAM966 gene, herein designated VGAM GENE, encodes a VGAM966 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM966 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM966 precursor RNA is designated SEQ ID:25506, and is provided hereinbelow with reference to the sequence listing part.

[13481] VGAM966 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM966 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13482] An enzyme complex designated DICER COMPLEX, dices the VGAM966 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM966 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM966 RNA is designated SEQ ID:25507, and is provided hereinbelow with reference to the sequence listing part.

[13483] VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[13484] VGAM966 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM966 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM966 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13485] The complementary binding of VGAM966 RNA, herein designated VGAM RNA, to host target binding sites on VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM966 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13486] It is appreciated that VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM966 host target genes. The mRNA of each one of this plurality of VGAM966 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM966 RNA, herein designated VGAM RNA, and which when bound by VGAM966 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM966 host target proteins.

[13487] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM966 gene, herein designated VGAM GENE, on one or

more VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13488] It is yet further appreciated that a function of VGAM966 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM966 correlate with, and may be deduced from, the identity of the host target genes which VGAM966 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[13489] Nucleotide sequences of the VGAM966 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM966 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM966 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM966 are further described hereinbelow with reference to Table 1.

[13490] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM966 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13491] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 967 (VGAM967) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13492] VGAM967 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM967 was detected is described

hereinabove with reference to Figs. 2–8.

[13493] VGAM967 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Citrus tristeza virus.

VGAM967 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13494] VGAM967 gene, herein designated VGAM GENE, encodes a VGAM967 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM967 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM967 precursor RNA is designated SEQ ID:25566, and is provided hereinbelow with reference to the sequence listing part.

[13495] VGAM967 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM967 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13496] An enzyme complex designated DICER COMPLEX, dices the VGAM967 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM967 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM967 RNA is designated SEQ ID:25567, and is provided hereinbelow with reference to the sequence listing part.

[13497] VGAM967 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13498] VGAM967 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM967 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM967 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13499] The complementary binding of VGAM967 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM967 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13500] It is appreciated that VGAM967 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM967 host target genes. The mRNA of each one of this plurality of VGAM967 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM967 RNA, herein designated VGAM RNA, and which when bound by VGAM967 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM967 host target proteins.

[13501] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM967 gene, herein designated VGAM GENE, on one or more VGAM967 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13502] It is yet further appreciated that a function of VGAM967 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM967 include diagnosis, prevention and treatment of viral infection by Citrus tristeza virus. Specific functions, and accordingly utilities, of VGAM967 correlate with, and may be deduced from, the identity of the host target genes which VGAM967 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13503] Nucleotide sequences of the VGAM967 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM967 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM967 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM967 are further described hereinbelow with reference to Table 1.

[13504] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM967 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13505] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 968 (VGAM968) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13506] VGAM968 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM968 was detected is described hereinabove with reference to Figs. 2-8.

[13507] VGAM968 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Citrus tristeza virus.

VGAM968 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13508] VGAM968 gene, herein designated VGAM GENE, encodes a VGAM968 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM968 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM968 precursor RNA is designated SEQ ID:25570, and is provided hereinbelow with reference to the sequence listing part.

[13509] VGAM968 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM968 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[13510] An enzyme complex designated DICER COMPLEX, dices the VGAM968 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM968 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM968 RNA is designated SEQ ID:25571, and is provided hereinbelow with reference to the sequence listing part.

[13511] VGAM968 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13512] VGAM968 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM968 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM968 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13513] The complementary binding of VGAM968 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM968 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13514] It is appreciated that VGAM968 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM968 host target genes. The mRNA of each one of this plurality of VGAM968 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM968 RNA, herein designated VGAM RNA, and which when bound by VGAM968 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM968 host target proteins.

[13515] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM968 gene, herein designated VGAM GENE, on one or more VGAM968 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13516] It is yet further appreciated that a function of VGAM968 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of viral infection by Citrus tristeza virus. Specific functions, and accordingly utilities, of VGAM968 correlate with, and may be deduced from, the identity of the host target genes which VGAM968 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13517] Nucleotide sequences of the VGAM968 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM968 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM968 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM968 are further described hereinbelow with reference to Table 1.

[13518] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM968 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13519] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 969 (VGAM969) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13520] VGAM969 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM969 was detected is described hereinabove with reference to Figs. 2-8.

[13521] VGAM969 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Citrus tristeza virus. VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13522] VGAM969 gene, herein designated VGAM GENE, encodes a VGAM969 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM969 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM969 precursor RNA is designated SEQ ID:25577, and is provided hereinbelow with reference to the sequence listing part.

[13523] VGAM969 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM969 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13524] An enzyme complex designated DICER COMPLEX, dices the VGAM969 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM969 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM969 RNA is designated SEQ ID:25578, and is provided hereinbelow with reference to the sequence listing part.

[13525] VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13526] VGAM969 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM969 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM969 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13527] The complementary binding of VGAM969 RNA, herein designated VGAM RNA, to host target binding sites on VGAM969 host target RNA, herein designated VGAM HOST



TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM969 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13528] It is appreciated that VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM969 host target genes. The mRNA of each one of this plurality of VGAM969 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM969 RNA, herein designated VGAM RNA, and which when bound by VGAM969 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM969 host target proteins.

[13529] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM969 gene, herein designated VGAM GENE, on one or more VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13530] It is yet further appreciated that a function of VGAM969 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM969 include diagnosis, prevention and treatment of viral infection by Citrus tristeza virus. Specific functions, and accordingly utilities, of VGAM969 correlate with, and may be deduced from, the identity of the host target genes which VGAM969 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13531] Nucleotide sequences of the VGAM969 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM969 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM969 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM969 are further described hereinbelow with reference to Table 1.

[13532] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM969 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13533] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 970 (VGAM970) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13534] VGAM970 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM970 was detected is described hereinabove with reference to Figs. 2-8.

[13535] VGAM970 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2.

VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13536] VGAM970 gene, herein designated VGAM GENE, encodes a VGAM970 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM970 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM970 precursor RNA is designated SEQ ID:25624, and is provided hereinbelow with reference to the sequence listing part.

[13537] VGAM970 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM970 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13538] An enzyme complex designated DICER COMPLEX, dices

the VGAM970 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM970 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM970 RNA is designated SEQ ID:25625, and is provided hereinbelow with reference to the sequence listing part.

[13539] VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13540] VGAM970 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM970 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM970 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM970 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13541] The complementary binding of VGAM970 RNA, herein designated VGAM RNA, to host target binding sites on VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM970 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13542] It is appreciated that VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM970 host target genes. The mRNA of each one of this plurality of VGAM970 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM970 RNA, herein designated VGAM RNA, and which when bound by VGAM970 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM970 host target proteins.

[13543] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM970 gene, herein designated VGAM GENE, on one or more VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13544] It is yet further appreciated that a function of VGAM970 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM970 correlate with, and may be deduced from, the identity of the host target genes which VGAM970 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13545] Nucleotide sequences of the VGAM970 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM970 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM970 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM970 are further described hereinbelow with reference to Table 1.

[13546] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM970 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13547] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 971 (VGAM971) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13548] VGAM971 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM971 was detected is described hereinabove with reference to Figs. 2-8.

[13549] VGAM971 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 12. VGAM971 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13550] VGAM971 gene, herein designated VGAM GENE, encodes a VGAM971 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM971 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM971 precursor RNA is designated SEQ ID:25674, and is provided hereinbelow with reference to the sequence listing part.

[13551] VGAM971 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM971 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13552] An enzyme complex designated DICER COMPLEX, dices the VGAM971 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM971 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM971 RNA is designated SEQ ID:25675, and is provided hereinbelow with reference to the sequence listing part.

[13553] VGAM971 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13554] VGAM971 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM971 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13555] The complementary binding of VGAM971 RNA, herein designated VGAM RNA, to host target binding sites on VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM971 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM971 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13556] It is appreciated that VGAM971 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM971 host target genes. The mRNA of each one of this plurality of VGAM971 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM971 RNA, herein designated VGAM RNA, and which when bound by VGAM971 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM971 host target proteins.

[13557] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM971 gene, herein designated VGAM GENE, on one or more VGAM971 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13558] It is yet further appreciated that a function of VGAM971 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 12. Specific functions, and accordingly utilities, of VGAM971 correlate with, and may be deduced from, the identity of the host target genes which VGAM971 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13559] Nucleotide sequences of the VGAM971 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM971 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM971 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM971 are further described hereinbelow with reference to Table 1.

[13560] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM971 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13561] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 972 (VGAM972) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13562] VGAM972 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM972 was detected is described hereinabove with reference to Figs. 2-8.

[13563] VGAM972 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[13564] VGAM972 gene, herein designated VGAM GENE, encodes a VGAM972 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM972 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM972 precursor RNA is designated SEQ ID:25696, and is provided hereinbelow with reference to the sequence listing part.

[13565] VGAM972 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM972 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13566] An enzyme complex designated DICER COMPLEX, dices the VGAM972 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM972 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM972 RNA is designated SEQ ID:25697, and is provided hereinbelow with reference to the sequence listing part.

[13567] VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13568] VGAM972 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM972 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM972 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13569] The complementary binding of VGAM972 RNA, herein designated VGAM RNA, to host target binding sites on VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM972 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13570] It is appreciated that VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM972 host target genes. The mRNA of each one of this plurality of VGAM972 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM972 RNA, herein designated VGAM RNA, and which when bound by VGAM972 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM972 host target proteins.

[13571] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM972 gene, herein designated VGAM GENE, on one or more VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13572] It is yet further appreciated that a function of VGAM972 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM972 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM972 correlate with, and may be deduced from, the identity of the host target genes which VGAM972 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13573] Nucleotide sequences of the VGAM972 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM972 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM972 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM972 are further de-

scribed hereinbelow with reference to Table 1.

[13574] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM972 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13575] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 973 (VGAM973) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13576] VGAM973 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM973 was detected is described hereinabove with reference to Figs. 2-8.

[13577] VGAM973 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 12. VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13578] VGAM973 gene, herein designated VGAM GENE, encodes a VGAM973 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM973 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM973 precursor RNA is designated SEQ ID:25700, and is provided hereinbelow with reference to the sequence listing part.

[13579] VGAM973 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM973 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13580] An enzyme complex designated DICER COMPLEX, dices the VGAM973 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM973 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM973 RNA is designated SEQ ID:25701, and is provided hereinbelow with reference to the sequence listing part.

[13581] VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13582] VGAM973 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM973 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM973 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13583] The complementary binding of VGAM973 RNA, herein designated VGAM RNA, to host target binding sites on VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM973 host target protein, herein designated



VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13584] It is appreciated that VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM973 host target genes. The mRNA of each one of this plurality of VGAM973 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM973 RNA, herein designated VGAM RNA, and which when bound by VGAM973 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM973 host target proteins.

[13585] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM973 gene, herein designated VGAM GENE, on one or more VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13586] It is yet further appreciated that a function of VGAM973 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM973 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 12. Specific functions, and accordingly utilities, of VGAM973 correlate with, and may be deduced from, the identity of the host target genes which VGAM973 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13587] Nucleotide sequences of the VGAM973 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM973 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM973 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM973 are further described hereinbelow with reference to Table 1.

[13588] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM973 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13589] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 974 (VGAM974) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13590] VGAM974 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM974 was detected is described hereinabove with reference to Figs. 2-8.

[13591] VGAM974 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 12. VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13592] VGAM974 gene, herein designated VGAM GENE, encodes a

VGAM974 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM974 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM974 precursor RNA is designated SEQ ID:25870, and is provided hereinbelow with reference to the sequence listing part.

[13593] VGAM974 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM974 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13594] An enzyme complex designated DICER COMPLEX, dices the VGAM974 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM974 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM974 RNA is designated SEQ ID:25871, and is provided hereinbelow with reference to the sequence listing part.

[13595] VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13596] VGAM974 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM974 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13597] The complementary binding of VGAM974 RNA, herein designated VGAM RNA, to host target binding sites on VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM974 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[13598] It is appreciated that VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM974 host target genes. The mRNA of each one of this plurality of VGAM974 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM974 RNA, herein designated VGAM RNA, and which when bound by VGAM974 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM974 host target proteins.

[13599] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM974 gene, herein designated VGAM GENE, on one or more VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13600] It is yet further appreciated that a function of VGAM974 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 12. Specific functions, and accordingly utilities, of VGAM974 correlate with, and may be deduced from, the identity of the host target genes which VGAM974 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13601] Nucleotide sequences of the VGAM974 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM974 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM974 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM974 are further described hereinbelow with reference to Table 1.

[13602] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM974 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13603] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 975 (VGAM975) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13604] VGAM975 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM975 was detected is described hereinabove with reference to Figs. 2-8.

[13605] VGAM975 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13606] VGAM975 gene, herein designated VGAM GENE, encodes a VGAM975 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM975 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM975 precursor RNA is designated SEQ ID:25912, and is provided hereinbelow with reference to the sequence listing part.

[13607] VGAM975 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM975 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13608] An enzyme complex designated DICER COMPLEX, dices the VGAM975 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM975 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM975 RNA is designated SEQ ID:25913, and is provided hereinbelow with reference to the sequence listing part.

[13609] VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13610] VGAM975 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM975 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13611] The complementary binding of VGAM975 RNA, herein designated VGAM RNA, to host target binding sites on VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM975 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13612] It is appreciated that VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM975 host target genes. The mRNA of each one of this plurality of VGAM975 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM975 RNA, herein designated VGAM RNA, and which when bound by VGAM975 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM975 host target proteins.

[13613] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM975 gene, herein designated VGAM GENE, on one or more VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13614] It is yet further appreciated that a function of VGAM975 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM975 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM975 correlate with, and may be deduced from, the identity of the host target genes which VGAM975 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13615] Nucleotide sequences of the VGAM975 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM975 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM975 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM975 are further described hereinbelow with reference to Table 1.

[13616] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM975 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13617] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 976 (VGAM976) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13618] VGAM976 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM976 was detected is described hereinabove with reference to Figs. 2–8.

[13619] VGAM976 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 83. VGAM976 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13620] VGAM976 gene, herein designated VGAM GENE, encodes a VGAM976 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike

most ordinary genes, VGAM976 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM976 precursor RNA is designated SEQ ID:25924, and is provided hereinbelow with reference to the sequence listing part.

[13621] VGAM976 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM976 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13622] An enzyme complex designated DICER COMPLEX, dices the VGAM976 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM976 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM976 RNA is designated SEQ ID:25925, and is provided hereinbelow with reference to the sequence listing part.

[13623] VGAM976 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13624] VGAM976 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM976 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM976 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13625] The complementary binding of VGAM976 RNA, herein designated VGAM RNA, to host target binding sites on VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM976 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13626] It is appreciated that VGAM976 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM976 host target genes. The mRNA of each one of this plurality of VGAM976 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM976 RNA, herein designated VGAM RNA, and which when bound by VGAM976 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM976 host target proteins.

[13627] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM976 gene, herein designated VGAM GENE, on one or more VGAM976 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13628] It is yet further appreciated that a function of VGAM976 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM976 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 83. Specific functions, and accordingly utilities, of VGAM976 correlate with, and may be deduced from, the identity of the host target genes which VGAM976 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13629] Nucleotide sequences of the VGAM976 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM976 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM976 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM976 are further described hereinbelow with reference to Table 1.

[13630] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM976 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13631] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 977 (VGAM977) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13632] VGAM977 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM977 was detected is described hereinabove with reference to Figs. 2–8.

[13633] VGAM977 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lucerne transient streak virus. VGAM977 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13634] VGAM977 gene, herein designated VGAM GENE, encodes a VGAM977 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM977 precursor RNA, herein

designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM977 precursor RNA is designated SEQ ID:25930, and is provided hereinbelow with reference to the sequence listing part.

[13635] VGAM977 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM977 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13636] An enzyme complex designated DICER COMPLEX, dices the VGAM977 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM977 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM977 RNA is designated SEQ ID:25931, and is provided hereinbelow with reference to the sequence listing part.

[13637] VGAM977 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13638] VGAM977 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM977 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13639] The complementary binding of VGAM977 RNA, herein designated VGAM RNA, to host target binding sites on VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM977 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13640] It is appreciated that VGAM977 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM977 host target genes. The mRNA of each one of this plurality of VGAM977 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM977 RNA, herein designated VGAM RNA, and which when bound by VGAM977 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM977 host target proteins.

[13641] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM977 gene, herein designated VGAM GENE, on one or more VGAM977 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[13642] It is yet further appreciated that a function of VGAM977 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of viral infection by Lucerne transient streak virus. Specific functions, and accordingly utilities, of VGAM977 correlate with, and may be deduced from, the identity of the host target genes which VGAM977 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13643] Nucleotide sequences of the VGAM977 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM977 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM977 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM977 are further described hereinbelow with reference to Table 1.

[13644] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM977 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13645] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 978 (VGAM978) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13646] VGAM978 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM978 was detected is described hereinabove with reference to Figs. 2–8.

[13647] VGAM978 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lucerne transient streak virus. VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13648] VGAM978 gene, herein designated VGAM GENE, encodes a VGAM978 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM978 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a

protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM978 precursor RNA is designated SEQ ID:25945, and is provided hereinbelow with reference to the sequence listing part.

[13649] VGAM978 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM978 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13650] An enzyme complex designated DICER COMPLEX, dices the VGAM978 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM978 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM978 RNA is designated SEQ ID:25946, and is provided hereinbelow with reference to the sequence listing part.

[13651] VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13652] VGAM978 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM978 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM978 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13653] The complementary binding of VGAM978 RNA, herein designated VGAM RNA, to host target binding sites on VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM978 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13654] It is appreciated that VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM978 host target genes. The mRNA of

each one of this plurality of VGAM978 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM978 RNA, herein designated VGAM RNA, and which when bound by VGAM978 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM978 host target proteins.

[13655] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM978 gene, herein designated VGAM GENE, on one or more VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[13656] It is yet further appreciated that a function of VGAM978 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM978 include diagnosis, prevention and treatment of viral infection by Lucerne transient streak virus. Specific functions, and accordingly utilities, of VGAM978 correlate with, and may be deduced from, the identity of the host target genes which VGAM978 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13657] Nucleotide sequences of the VGAM978 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM978 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM978 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM978 are further described hereinbelow with reference to Table 1.

[13658] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM978 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[13659] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 979 (VGAM979) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13660] VGAM979 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM979 was detected is described hereinabove with reference to Figs. 2–8.

[13661] VGAM979 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 30. VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13662] VGAM979 gene, herein designated VGAM GENE, encodes a VGAM979 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM979 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar

to the nucleotide sequence of VGAM979 precursor RNA is designated SEQ ID:25950, and is provided hereinbelow with reference to the sequence listing part.

[13663] VGAM979 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM979 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13664] An enzyme complex designated DICER COMPLEX, dices the VGAM979 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM979 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM979 RNA is designated SEQ ID:25951, and

is provided hereinbelow with reference to the sequence listing part.

[13665] VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13666] VGAM979 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM979 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM979 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13667] The complementary binding of VGAM979 RNA, herein designated VGAM RNA, to host target binding sites on VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM979 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13668] It is appreciated that VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM979 host target genes. The mRNA of each one of this plurality of VGAM979 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM979 RNA, herein designated VGAM RNA, and which when bound by VGAM979 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM979 host target proteins.

[13669] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM979 gene, herein designated VGAM GENE, on one or more VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13670] It is yet further appreciated that a function of VGAM979 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM979 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 30. Specific functions, and accordingly utilities, of VGAM979 correlate with, and may be deduced from, the identity of the host target genes which VGAM979 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13671] Nucleotide sequences of the VGAM979 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM979 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM979 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM979 are further described hereinbelow with reference to Table 1.

[13672] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM979 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13673] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 980 (VGAM980) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13674] VGAM980 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM980 was detected is described hereinabove with reference to Figs. 2–8.

[13675] VGAM980 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13676] VGAM980 gene, herein designated VGAM GENE, encodes a VGAM980 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM980 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM980 precursor RNA is

designated SEQ ID:25953, and is provided hereinbelow with reference to the sequence listing part.

[13677] VGAM980 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM980 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13678] An enzyme complex designated DICER COMPLEX, dices the VGAM980 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM980 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM980 RNA is designated SEQ ID:25954, and is provided hereinbelow with reference to the sequence



listing part.

[13679] VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13680] VGAM980 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM980 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM980 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13681] The complementary binding of VGAM980 RNA, herein designated VGAM RNA, to host target binding sites on VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM980 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13682] It is appreciated that VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM980 host target genes. The mRNA of each one of this plurality of VGAM980 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM980 RNA, herein designated VGAM RNA, and which when bound by VGAM980 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM980 host target proteins.

[13683] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM980 gene, herein designated VGAM GENE, on one or more VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13684] It is yet further appreciated that a function of VGAM980 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM980 include diagnosis, prevention and treatment of viral infection by *Amsacta moorei* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM980 correlate with, and may be deduced from, the identity of the host target genes which VGAM980 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13685] Nucleotide sequences of the VGAM980 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM980 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM980 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM980 are further described hereinbelow with reference to Table 1.

[13686] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM980 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13687] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 981 (VGAM981) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13688] VGAM981 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM981 was detected is described hereinabove with reference to Figs. 2–8.

[13689] VGAM981 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13690] VGAM981 gene, herein designated VGAM GENE, encodes a VGAM981 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM981 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM981 precursor RNA is designated SEQ ID:25967, and is provided hereinbelow

with reference to the sequence listing part.

[13691] VGAM981 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM981 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13692] An enzyme complex designated DICER COMPLEX, dices the VGAM981 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM981 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM981 RNA is designated SEQ ID:25968, and is provided hereinbelow with reference to the sequence listing part.

[13693] VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13694] VGAM981 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM981 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM981 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13695] The complementary binding of VGAM981 RNA, herein designated VGAM RNA, to host target binding sites on VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM981 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13696] It is appreciated that VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM981 host target genes. The mRNA of each one of this plurality of VGAM981 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM981 RNA, herein designated VGAM RNA, and which when bound by VGAM981 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM981 host target proteins.

[13697] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM981 gene, herein designated VGAM GENE, on one or more VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13698] It is yet further appreciated that a function of VGAM981 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM981 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM981 correlate with, and may be deduced from, the identity of the host target genes which VGAM981 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13699] Nucleotide sequences of the VGAM981 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM981 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM981 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM981 are further described hereinbelow with reference to Table 1.

[13700] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM981 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13701] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 982 (VGAM982) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13702] VGAM982 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM982 was detected is described hereinabove with reference to Figs. 2–8.

[13703] VGAM982 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine papillomavirus. VGAM982 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13704] VGAM982 gene, herein designated VGAM GENE, encodes a VGAM982 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM982 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM982 precursor RNA is designated SEQ ID:25980, and is provided hereinbelow with reference to the sequence listing part.

[13705] VGAM982 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM982 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13706] An enzyme complex designated DICER COMPLEX, dices the VGAM982 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM982 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM982 RNA is designated SEQ ID:25981, and is provided hereinbelow with reference to the sequence listing part.

[13707] VGAM982 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13708] VGAM982 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM982 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13709] The complementary binding of VGAM982 RNA, herein designated VGAM RNA, to host target binding sites on VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM982 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13710] It is appreciated that VGAM982 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM982 host target genes. The mRNA of each one of this plurality of VGAM982 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM982 RNA, herein designated VGAM

RNA, and which when bound by VGAM982 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM982 host target proteins.

[13711] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM982 gene, herein designated VGAM GENE, on one or more VGAM982 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13712] It is yet further appreciated that a function of VGAM982 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM982 include diagnosis, prevention and treatment of viral infection by Bovine papillomavirus. Specific functions, and accordingly utilities, of VGAM982 correlate with, and may be deduced from, the identity of the host target genes which VGAM982 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13713] Nucleotide sequences of the VGAM982 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM982 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM982 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM982 are further described hereinbelow with reference to Table 1.

[13714] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM982 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13715] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 983 (VGAM983) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13716] VGAM983 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM983 was detected is described hereinabove with reference to Figs. 2–8.

[13717] VGAM983 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine papillomavirus. VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13718] VGAM983 gene, herein designated VGAM GENE, encodes a VGAM983 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM983 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM983 precursor RNA is designated SEQ ID:26006, and is provided hereinbelow with reference to the sequence listing part.

[13719] VGAM983 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM983 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13720] An enzyme complex designated DICER COMPLEX, dices the VGAM983 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM983 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM983 RNA is designated SEQ ID:26007, and is provided hereinbelow with reference to the sequence listing part.

[13721] VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13722] VGAM983 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM983 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM983 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM983 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13723] The complementary binding of VGAM983 RNA, herein designated VGAM RNA, to host target binding sites on VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM983 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13724] It is appreciated that VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM983 host target genes. The mRNA of each one of this plurality of VGAM983 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM983 RNA, herein designated VGAM RNA, and which when bound by VGAM983 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM983 host target proteins.

[13725] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM983 gene, herein designated VGAM GENE, on one or more VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13726] It is yet further appreciated that a function of VGAM983 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM983 include diagnosis, prevention and

treatment of viral infection by Bovine papillomavirus. Specific functions, and accordingly utilities, of VGAM983 correlate with, and may be deduced from, the identity of the host target genes which VGAM983 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13727] Nucleotide sequences of the VGAM983 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM983 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM983 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM983 are further described hereinbelow with reference to Table 1.

[13728] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM983 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13729] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 984 (VGAM984) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13730] VGAM984 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM984 was detected is described hereinabove with reference to Figs. 2–8.

[13731] VGAM984 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine papillomavirus. VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13732] VGAM984 gene, herein designated VGAM GENE, encodes a VGAM984 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM984 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM984 precursor RNA is designated SEQ ID:26023, and is provided hereinbelow with reference to the sequence listing part.

[13733] VGAM984 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM984 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13734] An enzyme complex designated DICER COMPLEX, dices the VGAM984 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM984 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM984 RNA is designated SEQ ID:26024, and is provided hereinbelow with reference to the sequence listing part.

[13735] VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM984 host target RNA, herein designated VGAM



HOST TARGET RNA. VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13736] VGAM984 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM984 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM984 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13737] The complementary binding of VGAM984 RNA, herein designated VGAM RNA, to host target binding sites on VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM984 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13738] It is appreciated that VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM984 host target genes. The mRNA of each one of this plurality of VGAM984 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM984 RNA, herein designated VGAM RNA, and which when bound by VGAM984 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM984 host target proteins.

[13739] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM984 gene, herein designated VGAM GENE, on one or more VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13740] It is yet further appreciated that a function of VGAM984 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM984 include diagnosis, prevention and treatment of viral infection by Bovine papillomavirus. Spe-

cific functions, and accordingly utilities, of VGAM984 correlate with, and may be deduced from, the identity of the host target genes which VGAM984 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13741] Nucleotide sequences of the VGAM984 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM984 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM984 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM984 are further described hereinbelow with reference to Table 1.

[13742] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM984 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13743] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 985 (VGAM985) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[13744] VGAM985 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM985 was detected is described hereinabove with reference to Figs. 2–8.

[13745] VGAM985 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine papillomavirus. VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13746] VGAM985 gene, herein designated VGAM GENE, encodes a VGAM985 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM985 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM985 precursor RNA is designated SEQ ID:26028, and is provided hereinbelow with reference to the sequence listing part.

[13747] VGAM985 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM985 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13748] An enzyme complex designated DICER COMPLEX, dices the VGAM985 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM985 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM985 RNA is designated SEQ ID:26029, and is provided hereinbelow with reference to the sequence listing part.

[13749] VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM985 host target RNA, herein

designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13750] VGAM985 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM985 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13751] The complementary binding of VGAM985 RNA, herein designated VGAM RNA, to host target binding sites on VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM985 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13752] It is appreciated that VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM985 host target genes. The mRNA of each one of this plurality of VGAM985 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM985 RNA, herein designated VGAM RNA, and which when bound by VGAM985 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM985 host target proteins.



[13753] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM985 gene, herein designated VGAM GENE, on one or more VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13754] It is yet further appreciated that a function of VGAM985 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of viral infection by Bovine papillomavirus. Specific functions, and accordingly utilities, of VGAM985 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM985 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13755] Nucleotide sequences of the VGAM985 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM985 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM985 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM985 are further described hereinbelow with reference to Table 1.

[13756] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM985 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13757] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 986 (VGAM986) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[13758] VGAM986 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM986 was detected is described hereinabove with reference to Figs. 2–8.

[13759] VGAM986 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 2. VGAM986 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13760] VGAM986 gene, herein designated VGAM GENE, encodes a VGAM986 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM986 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM986 precursor RNA is designated SEQ ID:26051, and is provided hereinbelow with reference to the sequence listing part.

[13761] VGAM986 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM986 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13762] An enzyme complex designated DICER COMPLEX, dices the VGAM986 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM986 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM986 RNA is designated SEQ ID:26052, and is provided hereinbelow with reference to the sequence listing part.

[13763] VGAM986 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three re-

gions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13764] VGAM986 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM986 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM986 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13765] The complementary binding of VGAM986 RNA, herein designated VGAM RNA, to host target binding sites on VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM986 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13766] It is appreciated that VGAM986 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM986 host target genes. The mRNA of each one of this plurality of VGAM986 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM986 RNA, herein designated VGAM RNA, and which when bound by VGAM986 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM986 host target proteins.

[13767] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM986 gene, herein designated VGAM GENE, on one or more VGAM986 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13768] It is yet further appreciated that a function of VGAM986 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM986 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 2. Specific functions, and accordingly utilities, of VGAM986 correlate with, and may be deduced from, the identity of the

host target genes which VGAM986 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13769] Nucleotide sequences of the VGAM986 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM986 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM986 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM986 are further described hereinbelow with reference to Table 1.

[13770] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM986 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13771] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 987 (VGAM987) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[13772] VGAM987 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM987 was detected is described hereinabove with reference to Figs. 2–8.

[13773] VGAM987 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM987 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13774] VGAM987 gene, herein designated VGAM GENE, encodes a VGAM987 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM987 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM987 precursor RNA is designated SEQ ID:26124, and is provided hereinbelow with reference to the sequence listing part.

[13775] VGAM987 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM987 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13776] An enzyme complex designated DICER COMPLEX, dices the VGAM987 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM987 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM987 RNA is designated SEQ ID:26125, and is provided hereinbelow with reference to the sequence listing part.

[13777] VGAM987 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5

untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13778] VGAM987 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM987 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM987 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13779] The complementary binding of VGAM987 RNA, herein designated VGAM RNA, to host target binding sites on VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM987 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13780] It is appreciated that VGAM987 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM987 host target genes. The mRNA of each one of this plurality of VGAM987 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM987 RNA, herein designated VGAM RNA, and which when bound by VGAM987 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM987 host target proteins.

[13781] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM987 gene, herein designated VGAM GENE, on one or more VGAM987 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13782] It is yet further appreciated that a function of VGAM987 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM987 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM987 correlate with, and may be deduced from, the identity of the host target genes which VGAM987

binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13783] Nucleotide sequences of the VGAM987 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM987 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM987 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM987 are further described hereinbelow with reference to Table 1.

[13784] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM987 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13785] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 988 (VGAM988) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13786] VGAM988 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM988 was detected is described hereinabove with reference to Figs. 2–8.

[13787] VGAM988 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13788] VGAM988 gene, herein designated VGAM GENE, encodes a VGAM988 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM988 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM988 precursor RNA is designated SEQ ID:26128, and is provided hereinbelow with reference to the sequence listing part.

[13789] VGAM988 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM988 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13790] An enzyme complex designated DICER COMPLEX, dices the VGAM988 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM988 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM988 RNA is designated SEQ ID:26129, and is provided hereinbelow with reference to the sequence listing part.

[13791] VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 un-



translated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13792] VGAM988 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM988 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3'UTR and 5'UTR regions.

[13793] The complementary binding of VGAM988 RNA, herein designated VGAM RNA, to host target binding sites on VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM988 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13794] It is appreciated that VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM988 host target genes. The mRNA of each one of this plurality of VGAM988 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM988 RNA, herein designated VGAM RNA, and which when bound by VGAM988 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM988 host target proteins.

[13795] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM988 gene, herein designated VGAM GENE, on one or more VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13796] It is yet further appreciated that a function of VGAM988 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM988 correlate with, and may be deduced from, the identity of the host target genes which VGAM988 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[13797] Nucleotide sequences of the VGAM988 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM988 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM988 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM988 are further described hereinbelow with reference to Table 1.

[13798] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM988 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13799] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 989 (VGAM989) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13800] VGAM989 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM989 was detected is described hereinabove with reference to Figs. 2–8.

[13801] VGAM989 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13802] VGAM989 gene, herein designated VGAM GENE, encodes a VGAM989 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM989 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM989 precursor RNA is designated SEQ ID:26142, and is provided hereinbelow with reference to the sequence listing part.

[13803] VGAM989 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM989 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13804] An enzyme complex designated DICER COMPLEX, dices the VGAM989 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM989 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM989 RNA is designated SEQ ID:26143, and is provided hereinbelow with reference to the sequence listing part.

[13805] VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and

3UTR respectively.

[13806] VGAM989 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM989 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM989 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13807] The complementary binding of VGAM989 RNA, herein designated VGAM RNA, to host target binding sites on VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM989 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13808] It is appreciated that VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM989 host target genes. The mRNA of each one of this plurality of VGAM989 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM989 RNA, herein designated VGAM RNA, and which when bound by VGAM989 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM989 host target proteins.

[13809] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM989 gene, herein designated VGAM GENE, on one or



more VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13810] It is yet further appreciated that a function of VGAM989 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM989 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM989 correlate with, and may be deduced from, the identity of the host target genes which VGAM989 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13811] Nucleotide sequences of the VGAM989 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM989 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM989 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM989 are further described hereinbelow with reference to Table 1.

[13812] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM989 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13813] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 990 (VGAM990) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13814] VGAM990 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM990 was detected is described

hereinabove with reference to Figs. 2–8.

[13815] VGAM990 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3.

VGAM990 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13816] VGAM990 gene, herein designated VGAM GENE, encodes a VGAM990 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM990 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM990 precursor RNA is designated SEQ ID:26149, and is provided hereinbelow with reference to the sequence listing part.

[13817] VGAM990 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM990 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13818] An enzyme complex designated DICER COMPLEX, dices the VGAM990 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM990 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM990 RNA is designated SEQ ID:26150, and is provided hereinbelow with reference to the sequence listing part.

[13819] VGAM990 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13820] VGAM990 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM990 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13821] The complementary binding of VGAM990 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM990 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13822] It is appreciated that VGAM990 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM990 host target genes. The mRNA of each one of this plurality of VGAM990 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM990 RNA, herein designated VGAM RNA, and which when bound by VGAM990 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM990 host target proteins.

[13823] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM990 gene, herein designated VGAM GENE, on one or more VGAM990 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13824] It is yet further appreciated that a function of VGAM990 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM990 correlate with, and may be deduced from, the identity of the host target genes which VGAM990 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13825] Nucleotide sequences of the VGAM990 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM990 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM990 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM990 are further described hereinbelow with reference to Table 1.

[13826] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM990 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13827] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 991 (VGAM991) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13828] VGAM991 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM991 was detected is described hereinabove with reference to Figs. 2-8.



[13829] VGAM991 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM991 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13830] VGAM991 gene, herein designated VGAM GENE, encodes a VGAM991 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM991 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM991 precursor RNA is designated SEQ ID:26357, and is provided hereinbelow with reference to the sequence listing part.

[13831] VGAM991 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM991 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[13832] An enzyme complex designated DICER COMPLEX, dices the VGAM991 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM991 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM991 RNA is designated SEQ ID:26358, and is provided hereinbelow with reference to the sequence listing part.

[13833] VGAM991 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13834] VGAM991 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM991 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13835] The complementary binding of VGAM991 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM991 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13836] It is appreciated that VGAM991 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM991 host target genes. The mRNA of each one of this plurality of VGAM991 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM991 RNA, herein designated VGAM RNA, and which when bound by VGAM991 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM991 host target proteins.

[13837] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM991 gene, herein designated VGAM GENE, on one or more VGAM991 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13838] It is yet further appreciated that a function of VGAM991 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM991 correlate with, and may be deduced from, the identity of the host target genes which VGAM991 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13839] Nucleotide sequences of the VGAM991 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM991 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM991 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM991 are further described hereinbelow with reference to Table 1.

[13840] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM991 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13841] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 992 (VGAM992) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13842] VGAM992 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM992 was detected is described hereinabove with reference to Figs. 2-8.

[13843] VGAM992 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 7. VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13844] VGAM992 gene, herein designated VGAM GENE, encodes a VGAM992 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM992 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM992 precursor RNA is designated SEQ ID:26367, and is provided hereinbelow with reference to the sequence listing part.

[13845] VGAM992 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM992 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13846] An enzyme complex designated DICER COMPLEX, dices the VGAM992 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM992 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM992 RNA is designated SEQ ID:26368, and is provided hereinbelow with reference to the sequence listing part.

[13847] VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13848] VGAM992 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-



cated in untranslated regions of VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM992 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13849] The complementary binding of VGAM992 RNA, herein designated VGAM RNA, to host target binding sites on VGAM992 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM992 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13850] It is appreciated that VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM992 host target genes. The mRNA of each one of this plurality of VGAM992 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM992 RNA, herein designated VGAM RNA, and which when bound by VGAM992 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM992 host target proteins.

[13851] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM992 gene, herein designated VGAM GENE, on one or more VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13852] It is yet further appreciated that a function of VGAM992 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM992 correlate with, and may be deduced from, the identity of the host target genes which VGAM992 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13853] Nucleotide sequences of the VGAM992 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM992 RNA, herein designated VGAM RNA, and a

schematic representation of the secondary folding of VGAM992 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM992 are further described hereinbelow with reference to Table 1.

[13854] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM992 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13855] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 993 (VGAM993) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13856] VGAM993 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM993 was detected is described hereinabove with reference to Figs. 2-8.

[13857] VGAM993 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3.

VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13858] VGAM993 gene, herein designated VGAM GENE, encodes a VGAM993 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM993 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM993 precursor RNA is designated SEQ ID:26375, and is provided hereinbelow with reference to the sequence listing part.

[13859] VGAM993 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM993 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13860] An enzyme complex designated DICER COMPLEX, dices

the VGAM993 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM993 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM993 RNA is designated SEQ ID:26376, and is provided hereinbelow with reference to the sequence listing part.

[13861] VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13862] VGAM993 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM993 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM993 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13863] The complementary binding of VGAM993 RNA, herein designated VGAM RNA, to host target binding sites on VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM993 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13864] It is appreciated that VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM993 host target genes. The mRNA of each one of this plurality of VGAM993 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM993 RNA, herein designated VGAM RNA, and which when bound by VGAM993 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM993 host target proteins.

[13865] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM993 gene, herein designated VGAM GENE, on one or more VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13866] It is yet further appreciated that a function of VGAM993 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM993 correlate with, and may be deduced from, the identity of the host target genes which VGAM993 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13867] Nucleotide sequences of the VGAM993 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM993 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM993 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM993 are further described hereinbelow with reference to Table 1.

[13868] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM993 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13869] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 994 (VGAM994) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13870] VGAM994 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM994 was detected is described hereinabove with reference to Figs. 2-8.

[13871] VGAM994 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM994 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[13872] VGAM994 gene, herein designated VGAM GENE, encodes a VGAM994 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM994 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM994 precursor RNA is designated SEQ ID:26378, and is provided hereinbelow with reference to the sequence listing part.

[13873] VGAM994 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM994 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13874] An enzyme complex designated DICER COMPLEX, dices the VGAM994 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM994 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM994 RNA is designated SEQ ID:26379, and is provided hereinbelow with reference to the sequence listing part.

[13875] VGAM994 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13876] VGAM994 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM994 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM994 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13877] The complementary binding of VGAM994 RNA, herein designated VGAM RNA, to host target binding sites on VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM994 host tar-

get RNA, herein designated VGAM HOST TARGET RNA, into VGAM994 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13878] It is appreciated that VGAM994 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM994 host target genes. The mRNA of each one of this plurality of VGAM994 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM994 RNA, herein designated VGAM RNA, and which when bound by VGAM994 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM994 host target proteins.

[13879] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM994 gene, herein designated VGAM GENE, on one or more VGAM994 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13880] It is yet further appreciated that a function of VGAM994 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM994 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM994 correlate with, and may be deduced from, the identity of the host target genes which VGAM994 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13881] Nucleotide sequences of the VGAM994 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM994 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM994 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM994 are further described hereinbelow with reference to Table 1.

[13882] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM994 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13883] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 995 (VGAM995) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13884] VGAM995 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM995 was detected is described hereinabove with reference to Figs. 2-8.

[13885] VGAM995 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM995 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[13886] VGAM995 gene, herein designated VGAM GENE, encodes a VGAM995 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM995 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM995 precursor RNA is designated SEQ ID:26386, and is provided hereinbelow with reference to the sequence listing part.

[13887] VGAM995 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM995 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13888] An enzyme complex designated DICER COMPLEX, dices the VGAM995 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM995 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM995 RNA is designated SEQ ID:26387, and is provided hereinbelow with reference to the sequence listing part.

[13889] VGAM995 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13890] VGAM995 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM995 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM995 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13891] The complementary binding of VGAM995 RNA, herein designated VGAM RNA, to host target binding sites on VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA,

into VGAM995 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13892] It is appreciated that VGAM995 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM995 host target genes. The mRNA of each one of this plurality of VGAM995 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM995 RNA, herein designated VGAM RNA, and which when bound by VGAM995 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM995 host target proteins.

[13893] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM995 gene, herein designated VGAM GENE, on one or more VGAM995 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13894] It is yet further appreciated that a function of VGAM995 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM995 correlate with, and may be deduced from, the identity of the host target genes which VGAM995 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13895] Nucleotide sequences of the VGAM995 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM995 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM995 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM995 are further de-

scribed hereinbelow with reference to Table 1.

[13896] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM995 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13897] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 996 (VGAM996) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13898] VGAM996 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM996 was detected is described hereinabove with reference to Figs. 2-8.

[13899] VGAM996 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM996 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13900] VGAM996 gene, herein designated VGAM GENE, encodes a VGAM996 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM996 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM996 precursor RNA is designated SEQ ID:26446, and is provided hereinbelow with reference to the sequence listing part.

[13901] VGAM996 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM996 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13902] An enzyme complex designated DICER COMPLEX, dices the VGAM996 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM996 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM996 RNA is designated SEQ ID:26447, and is provided hereinbelow with reference to the sequence listing part.

[13903] VGAM996 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13904] VGAM996 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM996 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM996 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13905] The complementary binding of VGAM996 RNA, herein designated VGAM RNA, to host target binding sites on VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM996 host target protein, herein designated

VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13906] It is appreciated that VGAM996 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM996 host target genes. The mRNA of each one of this plurality of VGAM996 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM996 RNA, herein designated VGAM RNA, and which when bound by VGAM996 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM996 host target proteins.

[13907] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM996 gene, herein designated VGAM GENE, on one or more VGAM996 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13908] It is yet further appreciated that a function of VGAM996 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM996 correlate with, and may be deduced from, the identity of the host target genes which VGAM996 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13909] Nucleotide sequences of the VGAM996 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM996 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM996 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM996 are further described hereinbelow with reference to Table 1.

[13910] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM996 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13911] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 997 (VGAM997) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13912] VGAM997 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM997 was detected is described hereinabove with reference to Figs. 2-8.

[13913] VGAM997 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13914] VGAM997 gene, herein designated VGAM GENE, encodes a

VGAM997 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM997 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM997 precursor RNA is designated SEQ ID:26459, and is provided hereinbelow with reference to the sequence listing part.

[13915] VGAM997 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM997 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13916] An enzyme complex designated DICER COMPLEX, dices the VGAM997 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM997 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM997 RNA is designated SEQ ID:26460, and is provided hereinbelow with reference to the sequence listing part.

[13917] VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13918] VGAM997 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM997 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13919] The complementary binding of VGAM997 RNA, herein designated VGAM RNA, to host target binding sites on VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM997 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein

is therefore outlined by a broken line.

[13920] It is appreciated that VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM997 host target genes. The mRNA of each one of this plurality of VGAM997 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM997 RNA, herein designated VGAM RNA, and which when bound by VGAM997 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM997 host target proteins.

[13921] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM997 gene, herein designated VGAM GENE, on one or more VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13922] It is yet further appreciated that a function of VGAM997 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM997 correlate with, and may be deduced from, the identity of the host target genes which VGAM997 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13923] Nucleotide sequences of the VGAM997 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM997 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM997 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM997 are further described hereinbelow with reference to Table 1.

[13924] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM997 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13925] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 998 (VGAM998) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13926] VGAM998 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM998 was detected is described hereinabove with reference to Figs. 2-8.

[13927] VGAM998 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus D. VGAM998 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13928] VGAM998 gene, herein designated VGAM GENE, encodes a VGAM998 precursor RNA, herein designated VGAM PRE-

CURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM998 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM998 precursor RNA is designated SEQ ID:26474, and is provided hereinbelow with reference to the sequence listing part.

[13929] VGAM998 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM998 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13930] An enzyme complex designated DICER COMPLEX, dices the VGAM998 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM998 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM998 RNA is designated SEQ ID:26475, and is provided hereinbelow with reference to the sequence listing part.

[13931] VGAM998 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13932] VGAM998 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM998 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM998 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13933] The complementary binding of VGAM998 RNA, herein designated VGAM RNA, to host target binding sites on VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM998 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13934] It is appreciated that VGAM998 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM998 host target genes. The mRNA of each one of this plurality of VGAM998 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM998 RNA, herein designated VGAM RNA, and which when bound by VGAM998 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM998 host target proteins.

[13935] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM998 gene, herein designated VGAM GENE, on one or more VGAM998 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13936] It is yet further appreciated that a function of VGAM998 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM998 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus D. Specific functions, and accordingly utilities, of VGAM998 correlate with, and may be deduced from, the identity of the host target genes which VGAM998 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13937] Nucleotide sequences of the VGAM998 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM998 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM998 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM998 are further described hereinbelow with reference to Table 1.

[13938] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM998 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13939] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 999 (VGAM999) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13940] VGAM999 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM999 was detected is described hereinabove with reference to Figs. 2–8.

[13941] VGAM999 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus D. VGAM999 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13942] VGAM999 gene, herein designated VGAM GENE, encodes a VGAM999 precursor RNA, herein designated VGAM PRE-CURSOR RNA. Similar to other miRNA genes, and unlike



most ordinary genes, VGAM999 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM999 precursor RNA is designated SEQ ID:26478, and is provided hereinbelow with reference to the sequence listing part.

[13943] VGAM999 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM999 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13944] An enzyme complex designated DICER COMPLEX, dices the VGAM999 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM999 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM999 RNA is designated SEQ ID:26479, and is provided hereinbelow with reference to the sequence listing part.

[13945] VGAM999 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13946] VGAM999 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM999 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM999 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13947] The complementary binding of VGAM999 RNA, herein designated VGAM RNA, to host target binding sites on VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM999 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13948] It is appreciated that VGAM999 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM999 host target genes. The mRNA of each one of this plurality of VGAM999 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM999 RNA, herein designated VGAM RNA, and which when bound by VGAM999 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM999 host target proteins.

[13949] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM999 gene, herein designated VGAM GENE, on one or more VGAM999 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13950] It is yet further appreciated that a function of VGAM999 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM999 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus D. Specific functions, and accordingly utilities, of VGAM999 correlate with, and may be deduced from, the identity of the host target genes which VGAM999 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13951] Nucleotide sequences of the VGAM999 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM999 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM999 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM999 are further described hereinbelow with reference to Table 1.

[13952] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM999 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13953] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1000 (VGAM1000) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13954] VGAM1000 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1000 was detected is described hereinabove with reference to Figs. 2–8.

[13955] VGAM1000 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus D. VGAM1000 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13956] VGAM1000 gene, herein designated VGAM GENE, encodes a VGAM1000 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1000 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1000 precursor RNA is designated SEQ ID:26506, and is provided hereinbelow with reference to the sequence listing part.

[13957] VGAM1000 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1000 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13958] An enzyme complex designated DICER COMPLEX, dices the VGAM1000 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1000 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1000 RNA is designated SEQ ID:26507, and is provided hereinbelow with reference to the sequence listing part.

[13959] VGAM1000 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13960] VGAM1000 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1000 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13961] The complementary binding of VGAM1000 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1000 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13962] It is appreciated that VGAM1000 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1000 host target genes. The mRNA of each one of this plurality of VGAM1000 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1000 RNA, herein designated VGAM RNA, and which when bound by VGAM1000 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1000 host target proteins.

[13963] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1000 gene, herein designated VGAM GENE, on one or more VGAM1000 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[13964] It is yet further appreciated that a function of VGAM1000 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus D. Specific functions, and accordingly utilities, of VGAM1000 correlate with, and may be deduced from, the identity of the host target genes which VGAM1000 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13965] Nucleotide sequences of the VGAM1000 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1000 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1000 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1000 are further described hereinbelow with reference to Table 1.

[13966] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1000 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13967] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1001 (VGAM1001) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13968] VGAM1001 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1001 was detected is described hereinabove with reference to Figs. 2-8.

[13969] VGAM1001 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 14. VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13970] VGAM1001 gene, herein designated VGAM GENE, encodes a VGAM1001 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1001 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1001 precursor RNA is designated SEQ ID:26516, and is provided hereinbelow with reference to the sequence listing part.

[13971] VGAM1001 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1001 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13972] An enzyme complex designated DICER COMPLEX, dices the VGAM1001 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1001 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1001 RNA is designated SEQ ID:26517, and is provided hereinbelow with reference to the sequence listing part.

[13973] VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13974] VGAM1001 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1001 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13975] The complementary binding of VGAM1001 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1001 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13976] It is appreciated that VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1001 host target genes. The mRNA of

each one of this plurality of VGAM1001 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1001 RNA, herein designated VGAM RNA, and which when bound by VGAM1001 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1001 host target proteins.

[13977] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1001 gene, herein designated VGAM GENE, on one or more VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[13978] It is yet further appreciated that a function of VGAM1001 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 14. Specific functions, and accordingly utilities, of VGAM1001 correlate with, and may be deduced from, the identity of the host target genes which VGAM1001 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13979] Nucleotide sequences of the VGAM1001 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1001 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1001 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1001 are further described hereinbelow with reference to Table 1.

[13980] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1001 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[13981] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1002 (VGAM1002) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13982] VGAM1002 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1002 was detected is described hereinabove with reference to Figs. 2–8.

[13983] VGAM1002 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 14. VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13984] VGAM1002 gene, herein designated VGAM GENE, encodes a VGAM1002 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1002 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1002 precursor RNA is designated SEQ ID:26537, and is provided hereinbelow with reference to the sequence listing part.

[13985] VGAM1002 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1002 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13986] An enzyme complex designated DICER COMPLEX, dices the VGAM1002 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1002 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1002 RNA is designated SEQ ID:26538,

and is provided hereinbelow with reference to the sequence listing part.

[13987] VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[13988] VGAM1002 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1002 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1002 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[13989] The complementary binding of VGAM1002 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1002 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13990] It is appreciated that VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1002 host target genes. The mRNA of each one of this plurality of VGAM1002 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1002 RNA, herein designated VGAM RNA, and which when bound by VGAM1002 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1002 host target proteins.

[13991] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1002 gene, herein designated VGAM GENE, on one or more VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[13992] It is yet further appreciated that a function of VGAM1002 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1002 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 14. Specific functions, and accordingly utilities, of VGAM1002 correlate with, and may be deduced from, the identity of the host target genes which VGAM1002 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13993] Nucleotide sequences of the VGAM1002 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1002 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1002 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1002 are further described hereinbelow with reference to Table 1.

[13994] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1002 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13995] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1003 (VGAM1003) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13996] VGAM1003 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1003 was detected is described hereinabove with reference to Figs. 2–8.

[13997] VGAM1003 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 14. VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13998] VGAM1003 gene, herein designated VGAM GENE, encodes a VGAM1003 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1003 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1003 precu-



sor RNA is designated SEQ ID:26547, and is provided hereinbelow with reference to the sequence listing part.

[13999] VGAM1003 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1003 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14000] An enzyme complex designated DICER COMPLEX, dices the VGAM1003 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1003 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1003 RNA is designated SEQ ID:26548, and is provided hereinbelow with reference to the se-

quence listing part.

[14001] VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14002] VGAM1003 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1003 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14003] The complementary binding of VGAM1003 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1003 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14004] It is appreciated that VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1003 host target genes. The mRNA of each one of this plurality of VGAM1003 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1003 RNA, herein designated VGAM RNA, and which when bound by VGAM1003 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1003 host target proteins.

[14005] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1003 gene, herein designated VGAM GENE, on one or more VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14006] It is yet further appreciated that a function of VGAM1003

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 14. Specific functions, and accordingly utilities, of VGAM1003 correlate with, and may be deduced from, the identity of the host target genes which VGAM1003 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14007] Nucleotide sequences of the VGAM1003 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1003 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1003 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1003 are further described hereinbelow with reference to Table 1.

[14008] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1003 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14009] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1004 (VGAM1004) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14010] VGAM1004 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1004 was detected is described hereinabove with reference to Figs. 2–8.

[14011] VGAM1004 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14012] VGAM1004 gene, herein designated VGAM GENE, encodes a VGAM1004 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1004 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1004 precursor RNA is designated SEQ ID:26733, and is provided

hereinbelow with reference to the sequence listing part.

[14013] VGAM1004 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1004 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14014] An enzyme complex designated DICER COMPLEX, dices the VGAM1004 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1004 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1004 RNA is designated SEQ ID:26734, and is provided hereinbelow with reference to the sequence listing part.

[14015] VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14016] VGAM1004 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1004 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1004 RNA, herein designated



VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14017] The complementary binding of VGAM1004 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1004 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14018] It is appreciated that VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1004 host target genes. The mRNA of each one of this plurality of VGAM1004 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1004 RNA, herein designated VGAM RNA, and which when bound by VGAM1004 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1004 host target proteins.

[14019] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1004 gene, herein designated VGAM GENE, on one or more VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14020] It is yet further appreciated that a function of VGAM1004 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1004 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM1004 correlate with, and may be deduced from, the identity of the host target genes which VGAM1004 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14021] Nucleotide sequences of the VGAM1004 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1004 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1004 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1004 are further described hereinbelow with reference to Table 1.

[14022] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1004 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14023] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1005 (VGAM1005) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14024] VGAM1005 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1005 was detected is described hereinabove with reference to Figs. 2–8.

[14025] VGAM1005 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM1005 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14026] VGAM1005 gene, herein designated VGAM GENE, encodes a VGAM1005 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1005 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1005 precursor RNA is designated SEQ ID:26741, and is provided hereinbelow with reference to the sequence listing part.

[14027] VGAM1005 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1005 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14028] An enzyme complex designated DICER COMPLEX, dices the VGAM1005 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1005 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1005 RNA is designated SEQ ID:26742, and is provided hereinbelow with reference to the sequence listing part.

[14029] VGAM1005 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14030] VGAM1005 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1005 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14031] The complementary binding of VGAM1005 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1005 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14032] It is appreciated that VGAM1005 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1005 host target genes. The mRNA of each one of this plurality of VGAM1005 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1005 RNA, herein designated VGAM

RNA, and which when bound by VGAM1005 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1005 host target proteins.

[14033] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1005 gene, herein designated VGAM GENE, on one or more VGAM1005 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14034] It is yet further appreciated that a function of VGAM1005 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM1005 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM1005 correlate with, and may be deduced from, the identity of the host target genes which VGAM1005 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14035] Nucleotide sequences of the VGAM1005 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1005 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1005 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1005 are further described hereinbelow with reference to Table 1.

[14036] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1005 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14037] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1006 (VGAM1006) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14038] VGAM1006 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1006 was detected is described hereinabove with reference to Figs. 2-8.

[14039] VGAM1006 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14040] VGAM1006 gene, herein designated VGAM GENE, encodes a VGAM1006 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1006 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1006 precursor RNA is designated SEQ ID:26760, and is provided hereinbelow with reference to the sequence listing part.

[14041] VGAM1006 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1006 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14042] An enzyme complex designated DICER COMPLEX, dices the VGAM1006 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1006 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1006 RNA is designated SEQ ID:26761, and is provided hereinbelow with reference to the sequence listing part.

[14043] VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14044] VGAM1006 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1006 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1006 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14045] The complementary binding of VGAM1006 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1006 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14046] It is appreciated that VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1006 host target genes. The mRNA of each one of this plurality of VGAM1006 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1006 RNA, herein designated VGAM RNA, and which when bound by VGAM1006 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1006 host target proteins.

[14047] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1006 gene, herein designated VGAM GENE, on one or more VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14048] It is yet further appreciated that a function of VGAM1006 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1006 include diagnosis, prevention and

treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM1006 correlate with, and may be deduced from, the identity of the host target genes which VGAM1006 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14049] Nucleotide sequences of the VGAM1006 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1006 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1006 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1006 are further described hereinbelow with reference to Table 1.

[14050] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1006 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14051] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1007 (VGAM1007) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14052] VGAM1007 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1007 was detected is described hereinabove with reference to Figs. 2–8.

[14053] VGAM1007 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14054] VGAM1007 gene, herein designated VGAM GENE, encodes a VGAM1007 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1007 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1007 precursor RNA is designated SEQ ID:26810, and is provided hereinbelow with reference to the sequence listing part.

[14055] VGAM1007 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1007 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14056] An enzyme complex designated DICER COMPLEX, dices the VGAM1007 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1007 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1007 RNA is designated SEQ ID:26811, and is provided hereinbelow with reference to the sequence listing part.

[14057] VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1007 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14058] VGAM1007 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1007 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14059] The complementary binding of VGAM1007 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1007 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14060] It is appreciated that VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1007 host target genes. The mRNA of each one of this plurality of VGAM1007 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1007 RNA, herein designated VGAM RNA, and which when bound by VGAM1007 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1007 host target proteins.

[14061] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1007 gene, herein designated VGAM GENE, on one or more VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14062] It is yet further appreciated that a function of VGAM1007 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of viral infection by African swine fever virus.

Specific functions, and accordingly utilities, of VGAM1007 correlate with, and may be deduced from, the identity of the host target genes which VGAM1007 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14063] Nucleotide sequences of the VGAM1007 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1007 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1007 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1007 are further described hereinbelow with reference to Table 1.

[14064] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1007 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14065] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1008 (VGAM1008) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[14066] VGAM1008 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1008 was detected is described hereinabove with reference to Figs. 2–8.

[14067] VGAM1008 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14068] VGAM1008 gene, herein designated VGAM GENE, encodes a VGAM1008 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1008 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1008 precursor RNA is designated SEQ ID:26839, and is provided hereinbelow with reference to the sequence listing part.

[14069] VGAM1008 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1008 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14070] An enzyme complex designated DICER COMPLEX, dices the VGAM1008 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1008 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1008 RNA is designated SEQ ID:26840, and is provided hereinbelow with reference to the sequence listing part.

[14071] VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1008 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14072] VGAM1008 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1008 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1008 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14073] The complementary binding of VGAM1008 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1008 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14074] It is appreciated that VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1008 host target genes. The mRNA of each one of this plurality of VGAM1008 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1008 RNA, herein designated VGAM RNA, and which when bound by VGAM1008 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1008 host target proteins.

[14075] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1008 gene, herein designated VGAM GENE, on one or more VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14076] It is yet further appreciated that a function of VGAM1008 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1008

correlate with, and may be deduced from, the identity of the host target genes which VGAM1008 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14077] Nucleotide sequences of the VGAM1008 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1008 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1008 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1008 are further described hereinbelow with reference to Table 1.

[14078] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1008 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14079] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1009 (VGAM1009) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[14080] VGAM1009 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1009 was detected is described hereinabove with reference to Figs. 2–8.

[14081] VGAM1009 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola virus. VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14082] VGAM1009 gene, herein designated VGAM GENE, encodes a VGAM1009 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1009 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1009 precursor RNA is designated SEQ ID:26847, and is provided hereinbelow with reference to the sequence listing part.

[14083] VGAM1009 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1009 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14084] An enzyme complex designated DICER COMPLEX, dices the VGAM1009 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1009 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1009 RNA is designated SEQ ID:26848, and is provided hereinbelow with reference to the sequence listing part.

[14085] VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14086] VGAM1009 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1009 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1009 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14087] The complementary binding of VGAM1009 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1009 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14088] It is appreciated that VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1009 host target genes. The mRNA of each one of this plurality of VGAM1009 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1009 RNA, herein designated VGAM RNA, and which when bound by VGAM1009 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1009 host target proteins.

[14089] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1009 gene, herein designated VGAM GENE, on one or more VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14090] It is yet further appreciated that a function of VGAM1009 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1009 include diagnosis, prevention and treatment of viral infection by Variola virus. Specific functions, and accordingly utilities, of VGAM1009 correlate with, and may be deduced from, the identity of the host target genes which VGAM1009 binds and inhibits, and the



function of these host target genes, as elaborated herein–below.

[14091] Nucleotide sequences of the VGAM1009 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1009 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1009 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1009 are further described hereinbelow with reference to Table 1.

[14092] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1009 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14093] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1010 (VGAM1010) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14094] VGAM1010 is a novel bioinformatically detected regula–

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1010 was detected is described hereinabove with reference to Figs. 2–8.

[14095] VGAM1010 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14096] VGAM1010 gene, herein designated VGAM GENE, encodes a VGAM1010 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1010 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1010 precursor RNA is designated SEQ ID:26856, and is provided hereinbelow with reference to the sequence listing part.

[14097] VGAM1010 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1010 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14098] An enzyme complex designated DICER COMPLEX, dices the VGAM1010 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1010 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1010 RNA is designated SEQ ID:26857, and is provided hereinbelow with reference to the sequence listing part.

[14099] VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14100] VGAM1010 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1010 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[14101] The complementary binding of VGAM1010 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1010 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14102] It is appreciated that VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1010 host target genes. The mRNA of each one of this plurality of VGAM1010 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1010 RNA, herein designated VGAM RNA, and which when bound by VGAM1010 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1010 host target proteins.

[14103] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1010 gene, herein designated VGAM GENE, on one or more VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14104] It is yet further appreciated that a function of VGAM1010 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1010 correlate with, and may be deduced from, the identity of the host target genes which VGAM1010 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[14105] Nucleotide sequences of the VGAM1010 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1010 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1010 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1010 are further described hereinbelow with reference to Table 1.

[14106] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1010 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14107] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1011 (VGAM1011) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14108] VGAM1011 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1011 was detected is described hereinabove with reference to Figs. 2–8.

[14109] VGAM1011 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola virus. VGAM1011 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14110] VGAM1011 gene, herein designated VGAM GENE, encodes a VGAM1011 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1011 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1011 precursor RNA is designated SEQ ID:26865, and is provided hereinbelow with reference to the sequence listing part.

[14111] VGAM1011 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1011 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14112] An enzyme complex designated DICER COMPLEX, dices the VGAM1011 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1011 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1011 RNA is designated SEQ ID:26866, and is provided hereinbelow with reference to the sequence listing part.

[14113] VGAM1011 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14114] VGAM1011 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1011 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14115] The complementary binding of VGAM1011 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1011 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14116] It is appreciated that VGAM1011 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1011 host target genes. The mRNA of each one of this plurality of VGAM1011 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1011 RNA, herein designated VGAM RNA, and which when bound by VGAM1011 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1011 host target proteins.

[14117] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1011 gene, herein designated VGAM GENE, on one or more VGAM1011 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14118] It is yet further appreciated that a function of VGAM1011 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of viral infection by Variola virus. Specific functions, and accordingly utilities, of VGAM1011 correlate with, and may be deduced from, the identity of the host target genes which VGAM1011 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14119] Nucleotide sequences of the VGAM1011 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1011 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1011 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1011 are further described hereinbelow with reference to Table 1.

[14120] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1011 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14121] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1012 (VGAM1012) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14122] VGAM1012 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1012 was detected is described hereinabove with reference to Figs. 2-8.

[14123] VGAM1012 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aedes albopictus densovirus. VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14124] VGAM1012 gene, herein designated VGAM GENE, encodes a VGAM1012 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1012 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1012 precursor RNA is designated SEQ ID:26868, and is provided hereinbelow with reference to the sequence listing part.

[14125] VGAM1012 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1012 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[14126] An enzyme complex designated DICER COMPLEX, dices the VGAM1012 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1012 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1012 RNA is designated SEQ ID:26869, and is provided hereinbelow with reference to the sequence listing part.

[14127] VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14128] VGAM1012 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1012 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14129] The complementary binding of VGAM1012 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1012 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14130] It is appreciated that VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1012 host target genes. The mRNA of each one of this plurality of VGAM1012 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1012 RNA, herein designated VGAM RNA, and which when bound by VGAM1012 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1012 host target proteins.

[14131] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1012 gene, herein designated VGAM GENE, on one or more VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14132] It is yet further appreciated that a function of VGAM1012 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of viral infection by Aedes albopictus densovirus. Specific functions, and accordingly utilities, of VGAM1012 correlate with, and may be deduced from, the identity of the host target genes which VGAM1012 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14133] Nucleotide sequences of the VGAM1012 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1012 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1012 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1012 are further described hereinbelow with reference to Table 1.

[14134] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1012 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14135] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1013 (VGAM1013) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14136] VGAM1013 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1013 was detected is described hereinabove with reference to Figs. 2-8.

[14137] VGAM1013 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Aedes albopictus* densovirus. VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14138] VGAM1013 gene, herein designated VGAM GENE, encodes a VGAM1013 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1013 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1013 precursor RNA is designated SEQ ID:26928, and is provided hereinbelow with reference to the sequence listing part.

[14139] VGAM1013 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1013 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14140] An enzyme complex designated DICER COMPLEX, dices the VGAM1013 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1013 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1013 RNA is designated SEQ ID:26929, and is provided hereinbelow with reference to the sequence listing part.

[14141] VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14142] VGAM1013 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1013 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1013 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14143] The complementary binding of VGAM1013 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1013 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1013 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14144] It is appreciated that VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1013 host target genes. The mRNA of each one of this plurality of VGAM1013 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1013 RNA, herein designated VGAM RNA, and which when bound by VGAM1013 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1013 host target proteins.

[14145] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1013 gene, herein designated VGAM GENE, on one or more VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14146] It is yet further appreciated that a function of VGAM1013 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1013 include diagnosis, prevention and treatment of viral infection by Aedes albopictus densovirus. Specific functions, and accordingly utilities, of VGAM1013 correlate with, and may be deduced from, the identity of the host target genes which VGAM1013 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14147] Nucleotide sequences of the VGAM1013 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1013 RNA, herein designated VGAM RNA, and



a schematic representation of the secondary folding of VGAM1013 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1013 are further described hereinbelow with reference to Table 1.

[14148] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1013 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14149] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1014 (VGAM1014) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14150] VGAM1014 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1014 was detected is described hereinabove with reference to Figs. 2-8.

[14151] VGAM1014 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14152] VGAM1014 gene, herein designated VGAM GENE, encodes a VGAM1014 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1014 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1014 precursor RNA is designated SEQ ID:26931, and is provided hereinbelow with reference to the sequence listing part.

[14153] VGAM1014 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1014 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14154] An enzyme complex designated DICER COMPLEX, dices

the VGAM1014 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1014 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1014 RNA is designated SEQ ID:26932, and is provided hereinbelow with reference to the sequence listing part.

[14155] VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14156] VGAM1014 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1014 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1014 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1014 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14157] The complementary binding of VGAM1014 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1014 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14158] It is appreciated that VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1014 host target genes. The mRNA of each one of this plurality of VGAM1014 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1014 RNA, herein designated VGAM RNA, and which when bound by VGAM1014 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1014 host target proteins.

[14159] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1014 gene, herein designated VGAM GENE, on one or more VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14160] It is yet further appreciated that a function of VGAM1014 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1014 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1014 correlate with, and may be deduced from, the identity of the host target genes which VGAM1014 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14161] Nucleotide sequences of the VGAM1014 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1014 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1014 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1014 are further described hereinbelow with reference to Table 1.

[14162] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1014 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14163] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1015 (VGAM1015) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14164] VGAM1015 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1015 was detected is described hereinabove with reference to Figs. 2-8.

[14165] VGAM1015 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM1015 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[14166] VGAM1015 gene, herein designated VGAM GENE, encodes a VGAM1015 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1015 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1015 precursor RNA is designated SEQ ID:26939, and is provided hereinbelow with reference to the sequence listing part.

[14167] VGAM1015 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1015 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14168] An enzyme complex designated DICER COMPLEX, dices the VGAM1015 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM1015 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1015 RNA is designated SEQ ID:26940, and is provided hereinbelow with reference to the sequence listing part.

[14169] VGAM1015 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14170] VGAM1015 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1015 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1015 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14171] The complementary binding of VGAM1015 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1015

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1015 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14172] It is appreciated that VGAM1015 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1015 host target genes. The mRNA of each one of this plurality of VGAM1015 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1015 RNA, herein designated VGAM RNA, and which when bound by VGAM1015 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1015 host target proteins.

[14173] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1015 gene, herein designated VGAM GENE, on one or more VGAM1015 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14174] It is yet further appreciated that a function of VGAM1015 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1015 correlate with, and may be deduced from, the identity of the host target genes which VGAM1015 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14175] Nucleotide sequences of the VGAM1015 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1015 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1015 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1015 are further described hereinbelow with reference to Table 1.

[14176] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1015 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14177] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1016 (VGAM1016) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14178] VGAM1016 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1016 was detected is described hereinabove with reference to Figs. 2-8.

[14179] VGAM1016 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[14180] VGAM1016 gene, herein designated VGAM GENE, encodes a VGAM1016 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1016 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1016 precursor RNA is designated SEQ ID:26948, and is provided hereinbelow with reference to the sequence listing part.

[14181] VGAM1016 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1016 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14182] An enzyme complex designated DICER COMPLEX, dices the VGAM1016 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1016 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1016 RNA is designated SEQ ID:26949, and is provided hereinbelow with reference to the sequence listing part.

[14183] VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14184] VGAM1016 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1016 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14185] The complementary binding of VGAM1016 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1016 host target RNA, herein designated VGAM HOST TARGET



RNA, into VGAM1016 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14186] It is appreciated that VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1016 host target genes. The mRNA of each one of this plurality of VGAM1016 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1016 RNA, herein designated VGAM RNA, and which when bound by VGAM1016 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1016 host target proteins.

[14187] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1016 gene, herein designated VGAM GENE, on one or more VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14188] It is yet further appreciated that a function of VGAM1016 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1016 correlate with, and may be deduced from, the identity of the host target genes which VGAM1016 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14189] Nucleotide sequences of the VGAM1016 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1016 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1016 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1016 are further

described hereinbelow with reference to Table 1.

[14190] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1016 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14191] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1017 (VGAM1017) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14192] VGAM1017 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1017 was detected is described hereinabove with reference to Figs. 2-8.

[14193] VGAM1017 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice yellow mottle virus. VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14194] VGAM1017 gene, herein designated VGAM GENE, encodes a VGAM1017 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1017 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1017 precursor RNA is designated SEQ ID:26955, and is provided hereinbelow with reference to the sequence listing part.

[14195] VGAM1017 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1017 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14196] An enzyme complex designated DICER COMPLEX, dices the VGAM1017 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1017 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1017 RNA is designated SEQ ID:26956, and is provided hereinbelow with reference to the sequence listing part.

[14197] VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14198] VGAM1017 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1017 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1017 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14199] The complementary binding of VGAM1017 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1017 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14200] It is appreciated that VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1017 host target genes. The mRNA of each one of this plurality of VGAM1017 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1017 RNA, herein designated VGAM RNA, and which when bound by VGAM1017 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1017 host target proteins.

[14201] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1017 gene, herein designated VGAM GENE, on one or more VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14202] It is yet further appreciated that a function of VGAM1017 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of viral infection by Rice yellow mottle virus. Specific functions, and accordingly utilities, of VGAM1017 correlate with, and may be deduced from, the identity of the host target genes which VGAM1017 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14203] Nucleotide sequences of the VGAM1017 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1017 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1017 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1017 are further described hereinbelow with reference to Table 1.



[14204] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1017 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14205] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1018 (VGAM1018) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14206] VGAM1018 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1018 was detected is described hereinabove with reference to Figs. 2-8.

[14207] VGAM1018 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1018 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14208] VGAM1018 gene, herein designated VGAM GENE, encodes

a VGAM1018 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1018 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1018 precursor RNA is designated SEQ ID:26958, and is provided hereinbelow with reference to the sequence listing part.

[14209] VGAM1018 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1018 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14210] An enzyme complex designated DICER COMPLEX, dices the VGAM1018 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1018 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1018 RNA is designated SEQ ID:26959, and is provided hereinbelow with reference to the sequence listing part.

[14211] VGAM1018 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14212] VGAM1018 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1018 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1018 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14213] The complementary binding of VGAM1018 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1018 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[14214] It is appreciated that VGAM1018 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1018 host target genes. The mRNA of each one of this plurality of VGAM1018 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1018 RNA, herein designated VGAM RNA, and which when bound by VGAM1018 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1018 host target proteins.

[14215] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1018 gene, herein designated VGAM GENE, on one or more VGAM1018 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14216] It is yet further appreciated that a function of VGAM1018 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1018 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1018 correlate with, and may be deduced from, the identity of the host target genes which VGAM1018 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14217] Nucleotide sequences of the VGAM1018 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1018 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1018 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1018 are further described hereinbelow with reference to Table 1.

[14218] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1018 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14219] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1019 (VGAM1019) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14220] VGAM1019 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1019 was detected is described hereinabove with reference to Figs. 2-8.

[14221] VGAM1019 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14222] VGAM1019 gene, herein designated VGAM GENE, encodes a VGAM1019 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1019 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1019 precursor RNA is designated SEQ ID:26995, and is provided hereinbelow with reference to the sequence listing part.

[14223] VGAM1019 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1019 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14224] An enzyme complex designated DICER COMPLEX, dices the VGAM1019 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1019 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1019 RNA is designated SEQ ID:26996, and is provided hereinbelow with reference to the sequence listing part.

[14225] VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14226] VGAM1019 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1019 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14227] The complementary binding of VGAM1019 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1019 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14228] It is appreciated that VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1019 host target genes. The mRNA of each one of this plurality of VGAM1019 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1019 RNA, herein designated VGAM RNA, and which when bound by VGAM1019 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1019 host target proteins.

[14229] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1019 gene, herein designated VGAM GENE, on one or more VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14230] It is yet further appreciated that a function of VGAM1019 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1019 correlate with, and may be deduced from, the identity of the host target genes which VGAM1019 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14231] Nucleotide sequences of the VGAM1019 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1019 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1019 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1019 are further described hereinbelow with reference to Table 1.

[14232] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1019 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14233] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1020 (VGAM1020) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14234] VGAM1020 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1020 was detected is described hereinabove with reference to Figs. 2-8.

[14235] VGAM1020 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM1020 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14236] VGAM1020 gene, herein designated VGAM GENE, encodes a VGAM1020 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1020 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1020 precursor RNA is designated SEQ ID:27019, and is provided hereinbelow with reference to the sequence listing part.

[14237] VGAM1020 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1020 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14238] An enzyme complex designated DICER COMPLEX, dices the VGAM1020 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1020 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1020 RNA is designated SEQ ID:27020, and is provided hereinbelow with reference to the sequence listing part.

[14239] VGAM1020 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14240] VGAM1020 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1020 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14241] The complementary binding of VGAM1020 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1020 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14242] It is appreciated that VGAM1020 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1020 host target genes. The mRNA of each one of this plurality of VGAM1020 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1020 RNA, herein designated VGAM RNA, and which when bound by VGAM1020 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1020 host target proteins.

[14243] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1020 gene, herein designated VGAM GENE, on one or more VGAM1020 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14244] It is yet further appreciated that a function of VGAM1020 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM1020 correlate with, and may be deduced from, the identity of the host target genes which VGAM1020 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14245] Nucleotide sequences of the VGAM1020 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1020 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1020 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1020 are further described hereinbelow with reference to Table 1.

[14246] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1020 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14247] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1021 (VGAM1021) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14248] VGAM1021 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1021 was detected is described hereinabove with reference to Figs. 2–8.

[14249] VGAM1021 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lymphocystis disease virus 1. VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14250] VGAM1021 gene, herein designated VGAM GENE, encodes a VGAM1021 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1021 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1021 precursor RNA is designated SEQ ID:27029, and is provided hereinbelow with reference to the sequence listing part.

[14251] VGAM1021 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1021 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14252] An enzyme complex designated DICER COMPLEX, dices the VGAM1021 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1021 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1021 RNA is designated SEQ ID:27030, and is provided hereinbelow with reference to the sequence listing part.

[14253] VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14254] VGAM1021 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1021 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14255] The complementary binding of VGAM1021 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1021 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14256] It is appreciated that VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1021 host target genes. The mRNA of each one of this plurality of VGAM1021 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1021 RNA, herein designated VGAM RNA, and which when bound by VGAM1021 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1021 host target proteins.

[14257] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1021 gene, herein designated VGAM GENE, on one or more VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [14258] It is yet further appreciated that a function of VGAM1021 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of viral infection by Lymphocystis disease virus 1. Specific functions, and accordingly utilities, of VGAM1021 correlate with, and may be deduced from, the identity of the host target genes which VGAM1021 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [14259] Nucleotide sequences of the VGAM1021 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1021 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1021 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1021 are further described hereinbelow with reference to Table 1.
- [14260] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM1021 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14261] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1022 (VGAM1022) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14262] VGAM1022 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1022 was detected is described hereinabove with reference to Figs. 2-8.

[14263] VGAM1022 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14264] VGAM1022 gene, herein designated VGAM GENE, encodes a VGAM1022 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1022 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1022 precursor RNA is designated SEQ ID:27034, and is provided hereinbelow with reference to the sequence listing part.

[14265] VGAM1022 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1022 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14266] An enzyme complex designated DICER COMPLEX, dices the VGAM1022 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1022 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM1022 RNA is designated SEQ ID:27035, and is provided hereinbelow with reference to the sequence listing part.

[14267] VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14268] VGAM1022 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1022 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1022 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14269] The complementary binding of VGAM1022 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1022 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14270] It is appreciated that VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1022 host target genes. The mRNA of

each one of this plurality of VGAM1022 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1022 RNA, herein designated VGAM RNA, and which when bound by VGAM1022 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1022 host target proteins.

[14271] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1022 gene, herein designated VGAM GENE, on one or more VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[14272] It is yet further appreciated that a function of VGAM1022 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1022 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM1022 correlate with, and may be deduced from, the identity of the host target genes which VGAM1022 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14273] Nucleotide sequences of the VGAM1022 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1022 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1022 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1022 are further described hereinbelow with reference to Table 1.

[14274] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1022 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[14275] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1023 (VGAM1023) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14276] VGAM1023 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1023 was detected is described hereinabove with reference to Figs. 2–8.

[14277] VGAM1023 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM1023 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14278] VGAM1023 gene, herein designated VGAM GENE, encodes a VGAM1023 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1023 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1023 precursor RNA is designated SEQ ID:27044, and is provided hereinbelow with reference to the sequence listing part.

[14279] VGAM1023 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1023 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14280] An enzyme complex designated DICER COMPLEX, dices the VGAM1023 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1023 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1023 RNA is designated SEQ ID:27045,



and is provided hereinbelow with reference to the sequence listing part.

[14281] VGAM1023 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14282] VGAM1023 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1023 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14283] The complementary binding of VGAM1023 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1023 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14284] It is appreciated that VGAM1023 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1023 host target genes. The mRNA of each one of this plurality of VGAM1023 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1023 RNA, herein designated VGAM RNA, and which when bound by VGAM1023 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1023 host target proteins.

[14285] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1023 gene, herein designated VGAM GENE, on one or more VGAM1023 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14286] It is yet further appreciated that a function of VGAM1023 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM1023

correlate with, and may be deduced from, the identity of the host target genes which VGAM1023 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14287] Nucleotide sequences of the VGAM1023 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1023 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1023 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1023 are further described hereinbelow with reference to Table 1.

[14288] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1023 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14289] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1024 (VGAM1024) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[14290] VGAM1024 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1024 was detected is described hereinabove with reference to Figs. 2–8.

[14291] VGAM1024 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ground squirrel hepatitis virus. VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14292] VGAM1024 gene, herein designated VGAM GENE, encodes a VGAM1024 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1024 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1024 precursor RNA is designated SEQ ID:27049, and is provided hereinbelow with reference to the sequence listing part.

[14293] VGAM1024 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1024 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14294] An enzyme complex designated DICER COMPLEX, dices the VGAM1024 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1024 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1024 RNA is designated SEQ ID:27050, and is provided hereinbelow with reference to the sequence listing part.

[14295] VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14296] VGAM1024 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1024 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1024 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an



example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14297] The complementary binding of VGAM1024 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1024 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14298] It is appreciated that VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1024 host target genes. The mRNA of each one of this plurality of VGAM1024 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1024 RNA, herein designated VGAM RNA, and which when bound by VGAM1024 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1024 host target proteins.

[14299] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1024 gene, herein designated VGAM GENE, on one or more VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14300] It is yet further appreciated that a function of VGAM1024 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1024 include diagnosis, prevention and treatment of viral infection by Ground squirrel hepatitis virus. Specific functions, and accordingly utilities, of VGAM1024 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1024 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14301] Nucleotide sequences of the VGAM1024 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1024 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1024 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1024 are further described hereinbelow with reference to Table 1.

[14302] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1024 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14303] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1025 (VGAM1025) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14304] VGAM1025 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1025 was detected is described hereinabove with reference to Figs. 2–8.

[14305] VGAM1025 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ground squirrel hepatitis virus. VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14306] VGAM1025 gene, herein designated VGAM GENE, encodes a VGAM1025 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1025 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1025 precursor RNA is designated SEQ ID:27060, and is provided hereinbelow with reference to the sequence listing part.

[14307] VGAM1025 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1025 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14308] An enzyme complex designated DICER COMPLEX, dices the VGAM1025 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1025 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1025 RNA is designated SEQ ID:27061, and is provided hereinbelow with reference to the sequence listing part.

[14309] VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14310] VGAM1025 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1025 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14311] The complementary binding of VGAM1025 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1025 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14312] It is appreciated that VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1025 host target genes. The mRNA of each one of this plurality of VGAM1025 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1025 RNA, herein designated VGAM RNA, and which when bound by VGAM1025 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1025 host target proteins.

[14313] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1025 gene, herein designated VGAM GENE, on one or more VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14314] It is yet further appreciated that a function of VGAM1025 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of viral infection by Ground squirrel hepatitis virus. Specific functions, and accordingly utilities, of VGAM1025 correlate with, and may be deduced from, the identity of the host target genes which VGAM1025 binds



and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14315] Nucleotide sequences of the VGAM1025 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1025 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1025 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1025 are further described hereinbelow with reference to Table 1.

[14316] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1025 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14317] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1026 (VGAM1026) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14318] VGAM1026 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1026 was detected is described hereinabove with reference to Figs. 2–8.

[14319] VGAM1026 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14320] VGAM1026 gene, herein designated VGAM GENE, encodes a VGAM1026 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1026 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1026 precursor RNA is designated SEQ ID:27129, and is provided hereinbelow with reference to the sequence listing part.

[14321] VGAM1026 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1026 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14322] An enzyme complex designated DICER COMPLEX, dices the VGAM1026 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1026 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1026 RNA is designated SEQ ID:27130, and is provided hereinbelow with reference to the sequence listing part.

[14323] VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14324] VGAM1026 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1026 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[14325] The complementary binding of VGAM1026 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1026 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14326] It is appreciated that VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1026 host target genes. The mRNA of each one of this plurality of VGAM1026 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1026 RNA, herein designated VGAM RNA, and which when bound by VGAM1026 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1026 host target proteins.

[14327] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1026 gene, herein designated VGAM GENE, on one or more VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14328] It is yet further appreciated that a function of VGAM1026 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM1026 correlate with, and may be deduced from, the identity of the host target genes which VGAM1026 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[14329] Nucleotide sequences of the VGAM1026 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1026 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1026 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1026 are further described hereinbelow with reference to Table 1.

[14330] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1026 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14331] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1027 (VGAM1027) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14332] VGAM1027 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1027 was detected is described hereinabove with reference to Figs. 2–8.

[14333] VGAM1027 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14334] VGAM1027 gene, herein designated VGAM GENE, encodes a VGAM1027 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1027 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1027 precursor RNA is designated SEQ ID:27187, and is provided hereinbelow with reference to the sequence listing part.

[14335] VGAM1027 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1027 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the



RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14336] An enzyme complex designated DICER COMPLEX, dices the VGAM1027 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1027 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1027 RNA is designated SEQ ID:27188, and is provided hereinbelow with reference to the sequence listing part.

[14337] VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[14338] VGAM1027 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1027 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14339] The complementary binding of VGAM1027 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1027 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14340] It is appreciated that VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1027 host target genes. The mRNA of each one of this plurality of VGAM1027 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1027 RNA, herein designated VGAM RNA, and which when bound by VGAM1027 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1027 host target proteins.

[14341] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1027 gene, herein designated VGAM GENE, on one

or more VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14342] It is yet further appreciated that a function of VGAM1027 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM1027 correlate with, and may be deduced from, the identity of the host target genes which VGAM1027 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14343] Nucleotide sequences of the VGAM1027 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1027 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1027 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1027 are further described hereinbelow with reference to Table 1.

[14344] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1027 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14345] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1028 (VGAM1028) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14346] VGAM1028 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1028 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[14347] VGAM1028 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2.

VGAM1028 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14348] VGAM1028 gene, herein designated VGAM GENE, encodes a VGAM1028 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1028 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1028 precursor RNA is designated SEQ ID:27195, and is provided hereinbelow with reference to the sequence listing part.

[14349] VGAM1028 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1028 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14350] An enzyme complex designated DICER COMPLEX, dices the VGAM1028 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1028 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1028 RNA is designated SEQ ID:27196, and is provided hereinbelow with reference to the sequence listing part.

[14351] VGAM1028 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14352] VGAM1028 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1028 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1028 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14353] The complementary binding of VGAM1028 RNA, herein



designated VGAM RNA, to host target binding sites on VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1028 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14354] It is appreciated that VGAM1028 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1028 host target genes. The mRNA of each one of this plurality of VGAM1028 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1028 RNA, herein designated VGAM RNA, and which when bound by VGAM1028 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1028 host target proteins.

[14355] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1028 gene, herein designated VGAM GENE, on one or more VGAM1028 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14356] It is yet further appreciated that a function of VGAM1028 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1028 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1028 correlate with, and may be deduced from, the identity of the host target genes which VGAM1028 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14357] Nucleotide sequences of the VGAM1028 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1028 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1028 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1028 are further described hereinbelow with reference to Table 1.

[14358] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1028 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14359] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1029 (VGAM1029) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14360] VGAM1029 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1029 was detected is described hereinabove with reference to Figs. 2-8.

[14361] VGAM1029 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1029 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14362] VGAM1029 gene, herein designated VGAM GENE, encodes a VGAM1029 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1029 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1029 precursor RNA is designated SEQ ID:27208, and is provided hereinbelow with reference to the sequence listing part.

[14363] VGAM1029 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1029 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[14364] An enzyme complex designated DICER COMPLEX, dices the VGAM1029 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1029 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1029 RNA is designated SEQ ID:27209, and is provided hereinbelow with reference to the sequence listing part.

[14365] VGAM1029 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14366] VGAM1029 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1029 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14367] The complementary binding of VGAM1029 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1029 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14368] It is appreciated that VGAM1029 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1029 host target genes. The mRNA of each one of this plurality of VGAM1029 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1029 RNA, herein designated VGAM RNA, and which when bound by VGAM1029 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1029 host target proteins.

[14369] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1029 gene, herein designated VGAM GENE, on one or more VGAM1029 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14370] It is yet further appreciated that a function of VGAM1029 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1029 correlate with, and may be deduced from, the identity of the host target genes which VGAM1029 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14371] Nucleotide sequences of the VGAM1029 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



diced VGAM1029 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1029 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1029 are further described hereinbelow with reference to Table 1.

[14372] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1029 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14373] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1030 (VGAM1030) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14374] VGAM1030 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1030 was detected is described hereinabove with reference to Figs. 2-8.

[14375] VGAM1030 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 6. VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14376] VGAM1030 gene, herein designated VGAM GENE, encodes a VGAM1030 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1030 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1030 precursor RNA is designated SEQ ID:27235, and is provided hereinbelow with reference to the sequence listing part.

[14377] VGAM1030 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1030 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14378] An enzyme complex designated DICER COMPLEX, dices the VGAM1030 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1030 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1030 RNA is designated SEQ ID:27236, and is provided hereinbelow with reference to the sequence listing part.

[14379] VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14380] VGAM1030 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1030 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14381] The complementary binding of VGAM1030 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1030 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1030 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14382] It is appreciated that VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1030 host target genes. The mRNA of each one of this plurality of VGAM1030 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1030 RNA, herein designated VGAM RNA, and which when bound by VGAM1030 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1030 host target proteins.

[14383] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1030 gene, herein designated VGAM GENE, on one or more VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14384] It is yet further appreciated that a function of VGAM1030 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1030 correlate with, and may be deduced from, the identity of the host target genes which VGAM1030 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14385] Nucleotide sequences of the VGAM1030 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1030 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1030 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1030 are further described hereinbelow with reference to Table 1.

[14386] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1030 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14387] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1031 (VGAM1031) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14388] VGAM1031 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1031 was detected is described hereinabove with reference to Figs. 2-8.

[14389] VGAM1031 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6.

VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14390] VGAM1031 gene, herein designated VGAM GENE, encodes a VGAM1031 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1031 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1031 precursor RNA is designated SEQ ID:27243, and is provided hereinbelow with reference to the sequence listing part.

[14391] VGAM1031 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1031 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14392] An enzyme complex designated DICER COMPLEX, dices



the VGAM1031 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1031 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1031 RNA is designated SEQ ID:27130, and is provided hereinbelow with reference to the sequence listing part.

[14393] VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14394] VGAM1031 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1031 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1031 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1031 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14395] The complementary binding of VGAM1031 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1031 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14396] It is appreciated that VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1031 host target genes. The mRNA of each one of this plurality of VGAM1031 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1031 RNA, herein designated VGAM RNA, and which when bound by VGAM1031 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1031 host target proteins.

[14397] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1031 gene, herein designated VGAM GENE, on one or more VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14398] It is yet further appreciated that a function of VGAM1031 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1031 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1031 correlate with, and may be deduced from, the identity of the host target genes which VGAM1031 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14399] Nucleotide sequences of the VGAM1031 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1031 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1031 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1031 are further described hereinbelow with reference to Table 1.

[14400] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1031 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14401] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1032 (VGAM1032) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14402] VGAM1032 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1032 was detected is described hereinabove with reference to Figs. 2-8.

[14403] VGAM1032 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1032 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[14404] VGAM1032 gene, herein designated VGAM GENE, encodes a VGAM1032 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1032 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1032 precursor RNA is designated SEQ ID:27244, and is provided hereinbelow with reference to the sequence listing part.

[14405] VGAM1032 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1032 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14406] An enzyme complex designated DICER COMPLEX, dices the VGAM1032 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1032 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1032 RNA is designated SEQ ID:27245, and is provided hereinbelow with reference to the sequence listing part.

[14407] VGAM1032 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1032 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1032 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14408] VGAM1032 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1032 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1032 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1032 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14409] The complementary binding of VGAM1032 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1032 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1032



host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1032 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14410] It is appreciated that VGAM1032 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1032 host target genes. The mRNA of each one of this plurality of VGAM1032 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1032 RNA, herein designated VGAM RNA, and which when bound by VGAM1032 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1032 host target proteins.

[14411] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1032 gene, herein designated VGAM GENE, on one or more VGAM1032 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14412] It is yet further appreciated that a function of VGAM1032 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1032 correlate with, and may be deduced from, the identity of the host target genes which VGAM1032 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14413] Nucleotide sequences of the VGAM1032 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1032 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1032 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1032 are further described hereinbelow with reference to Table 1.

[14414] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1032 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14415] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1033 (VGAM1033) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14416] VGAM1033 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1033 was detected is described hereinabove with reference to Figs. 2-8.

[14417] VGAM1033 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[14418] VGAM1033 gene, herein designated VGAM GENE, encodes a VGAM1033 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1033 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1033 precursor RNA is designated SEQ ID:27252, and is provided hereinbelow with reference to the sequence listing part.

[14419] VGAM1033 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1033 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14420] An enzyme complex designated DICER COMPLEX, dices the VGAM1033 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1033 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1033 RNA is designated SEQ ID:27253, and is provided hereinbelow with reference to the sequence listing part.

[14421] VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14422] VGAM1033 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1033 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14423] The complementary binding of VGAM1033 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1033 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1033 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14424] It is appreciated that VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1033 host target genes. The mRNA of each one of this plurality of VGAM1033 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1033 RNA, herein designated VGAM RNA, and which when bound by VGAM1033 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1033 host target proteins.

[14425] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1033 gene, herein designated VGAM GENE, on one or more VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14426] It is yet further appreciated that a function of VGAM1033 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1033 correlate with, and may be deduced from, the identity of the host target genes which VGAM1033 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14427] Nucleotide sequences of the VGAM1033 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1033 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1033 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1033 are further



described hereinbelow with reference to Table 1.

[14428] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1033 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14429] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1034 (VGAM1034) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14430] VGAM1034 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1034 was detected is described hereinabove with reference to Figs. 2-8.

[14431] VGAM1034 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14432] VGAM1034 gene, herein designated VGAM GENE, encodes a VGAM1034 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1034 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1034 precursor RNA is designated SEQ ID:27267, and is provided hereinbelow with reference to the sequence listing part.

[14433] VGAM1034 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1034 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14434] An enzyme complex designated DICER COMPLEX, dices the VGAM1034 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1034 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1034 RNA is designated SEQ ID:27268, and is provided hereinbelow with reference to the sequence listing part.

[14435] VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14436] VGAM1034 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1034 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1034 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14437] The complementary binding of VGAM1034 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1034 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14438] It is appreciated that VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1034 host target genes. The mRNA of each one of this plurality of VGAM1034 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1034 RNA, herein designated VGAM RNA, and which when bound by VGAM1034 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1034 host target proteins.

[14439] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1034 gene, herein designated VGAM GENE, on one or more VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14440] It is yet further appreciated that a function of VGAM1034 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1034 correlate with, and may be deduced from, the identity of the host target genes which VGAM1034 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14441] Nucleotide sequences of the VGAM1034 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1034 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1034 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1034 are further described hereinbelow with reference to Table 1.

[14442] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1034 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14443] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1035 (VGAM1035) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14444] VGAM1035 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1035 was detected is described hereinabove with reference to Figs. 2-8.

[14445] VGAM1035 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 52. VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14446] VGAM1035 gene, herein designated VGAM GENE, encodes

a VGAM1035 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1035 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1035 precursor RNA is designated SEQ ID:27271, and is provided hereinbelow with reference to the sequence listing part.

[14447] VGAM1035 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1035 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14448] An enzyme complex designated DICER COMPLEX, dices the VGAM1035 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1035 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1035 RNA is designated SEQ ID:27272, and is provided hereinbelow with reference to the sequence listing part.

[14449] VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14450] VGAM1035 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1035 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1035 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14451] The complementary binding of VGAM1035 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1035 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[14452] It is appreciated that VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1035 host target genes. The mRNA of each one of this plurality of VGAM1035 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1035 RNA, herein designated VGAM RNA, and which when bound by VGAM1035 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1035 host target proteins.

[14453] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1035 gene, herein designated VGAM GENE, on one or more VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14454] It is yet further appreciated that a function of VGAM1035 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1035 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 52. Specific functions, and accordingly utilities, of VGAM1035 correlate with, and may be deduced from, the identity of the host target genes which VGAM1035 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14455] Nucleotide sequences of the VGAM1035 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1035 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1035 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1035 are further described hereinbelow with reference to Table 1.

[14456] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1035 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14457] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1036 (VGAM1036) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14458] VGAM1036 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1036 was detected is described hereinabove with reference to Figs. 2-8.

[14459] VGAM1036 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14460] VGAM1036 gene, herein designated VGAM GENE, encodes a VGAM1036 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1036 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1036 precursor RNA is designated SEQ ID:27302, and is provided hereinbelow with reference to the sequence listing part.

[14461] VGAM1036 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1036 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14462] An enzyme complex designated DICER COMPLEX, dices the VGAM1036 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1036 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1036 RNA is designated SEQ ID:27303, and is provided hereinbelow with reference to the sequence listing part.

[14463] VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14464] VGAM1036 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1036 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14465] The complementary binding of VGAM1036 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1036 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[14466] It is appreciated that VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1036 host target genes. The mRNA of each one of this plurality of VGAM1036 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1036 RNA, herein designated VGAM RNA, and which when bound by VGAM1036 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1036 host target proteins.

[14467] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1036 gene, herein designated VGAM GENE, on one or more VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14468] It is yet further appreciated that a function of VGAM1036 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1036 correlate with, and may be deduced from, the identity of the host target genes which VGAM1036 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14469] Nucleotide sequences of the VGAM1036 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1036 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1036 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1036 are further described hereinbelow with reference to Table 1.

[14470] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1036 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14471] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1037 (VGAM1037) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14472] VGAM1037 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1037 was detected is described hereinabove with reference to Figs. 2-8.

[14473] VGAM1037 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1037 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14474] VGAM1037 gene, herein designated VGAM GENE, encodes a VGAM1037 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1037 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1037 precursor RNA is designated SEQ ID:27309, and is provided hereinbelow with reference to the sequence listing part.

[14475] VGAM1037 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1037 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14476] An enzyme complex designated DICER COMPLEX, dices the VGAM1037 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1037 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1037 RNA is designated SEQ ID:27310, and is provided hereinbelow with reference to the sequence listing part.

[14477] VGAM1037 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14478] VGAM1037 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1037 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1037 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14479] The complementary binding of VGAM1037 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1037 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14480] It is appreciated that VGAM1037 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1037 host target genes. The mRNA of each one of this plurality of VGAM1037 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1037 RNA, herein designated VGAM RNA, and which when bound by VGAM1037 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1037 host target proteins.

[14481] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1037 gene, herein designated VGAM GENE, on one or more VGAM1037 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14482] It is yet further appreciated that a function of VGAM1037 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1037 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1037 correlate with, and may be deduced from, the identity of the host target genes which VGAM1037 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14483] Nucleotide sequences of the VGAM1037 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1037 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1037 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1037 are further described hereinbelow with reference to Table 1.

[14484] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the



complementarity of each of these host target binding sites to VGAM1037 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14485] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1038 (VGAM1038) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14486] VGAM1038 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1038 was detected is described hereinabove with reference to Figs. 2–8.

[14487] VGAM1038 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 52. VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14488] VGAM1038 gene, herein designated VGAM GENE, encodes a VGAM1038 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1038 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1038 precursor RNA is designated SEQ ID:27321, and is provided hereinbelow with reference to the sequence listing part.

[14489] VGAM1038 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1038 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14490] An enzyme complex designated DICER COMPLEX, dices the VGAM1038 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1038 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1038 RNA is designated SEQ ID:27322, and is provided hereinbelow with reference to the sequence listing part.

[14491] VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14492] VGAM1038 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1038 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14493] The complementary binding of VGAM1038 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1038 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14494] It is appreciated that VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1038 host target genes. The mRNA of each one of this plurality of VGAM1038 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1038 RNA, herein designated VGAM RNA, and which when bound by VGAM1038 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1038 host target proteins.

[14495] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1038 gene, herein designated VGAM GENE, on one or more VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [14496] It is yet further appreciated that a function of VGAM1038 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 52. Specific functions, and accordingly utilities, of VGAM1038 correlate with, and may be deduced from, the identity of the host target genes which VGAM1038 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [14497] Nucleotide sequences of the VGAM1038 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1038 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1038 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1038 are further described hereinbelow with reference to Table 1.
- [14498] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1038 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14499] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1039 (VGAM1039) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14500] VGAM1039 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1039 was detected is described hereinabove with reference to Figs. 2-8.

[14501] VGAM1039 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14502] VGAM1039 gene, herein designated VGAM GENE, encodes a VGAM1039 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1039 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1039 precursor RNA is designated SEQ ID:27331, and is provided hereinbelow with reference to the sequence listing part.

[14503] VGAM1039 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1039 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14504] An enzyme complex designated DICER COMPLEX, dices the VGAM1039 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1039 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-



quence of VGAM1039 RNA is designated SEQ ID:27332, and is provided hereinbelow with reference to the sequence listing part.

[14505] VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14506] VGAM1039 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1039 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14507] The complementary binding of VGAM1039 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1039 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14508] It is appreciated that VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1039 host target genes. The mRNA of

each one of this plurality of VGAM1039 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1039 RNA, herein designated VGAM RNA, and which when bound by VGAM1039 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1039 host target proteins.

[14509] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1039 gene, herein designated VGAM GENE, on one or more VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[14510] It is yet further appreciated that a function of VGAM1039 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1039 correlate with, and may be deduced from, the identity of the host target genes which VGAM1039 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14511] Nucleotide sequences of the VGAM1039 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1039 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1039 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1039 are further described hereinbelow with reference to Table 1.

[14512] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1039 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[14513] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1040 (VGAM1040) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14514] VGAM1040 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1040 was detected is described hereinabove with reference to Figs. 2–8.

[14515] VGAM1040 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 3. VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14516] VGAM1040 gene, herein designated VGAM GENE, encodes a VGAM1040 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1040 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1040 precursor RNA is designated SEQ ID:27362, and is provided hereinbelow with reference to the sequence listing part.

[14517] VGAM1040 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1040 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14518] An enzyme complex designated DICER COMPLEX, dices the VGAM1040 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1040 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1040 RNA is designated SEQ ID:27363,

and is provided hereinbelow with reference to the sequence listing part.

[14519] VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14520] VGAM1040 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1040 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1040 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14521] The complementary binding of VGAM1040 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1040 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14522] It is appreciated that VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1040 host target genes. The mRNA of each one of this plurality of VGAM1040 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1040 RNA, herein designated VGAM RNA, and which when bound by VGAM1040 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1040 host target proteins.

[14523] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1040 gene, herein designated VGAM GENE, on one or more VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14524] It is yet further appreciated that a function of VGAM1040 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1040 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1040 correlate with, and may be deduced from, the identity of the host target genes which VGAM1040 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14525] Nucleotide sequences of the VGAM1040 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1040 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1040 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1040 are further described hereinbelow with reference to Table 1.

[14526] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1040 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14527] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1041 (VGAM1041) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14528] VGAM1041 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1041 was detected is described hereinabove with reference to Figs. 2–8.

[14529] VGAM1041 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 3. VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14530] VGAM1041 gene, herein designated VGAM GENE, encodes a VGAM1041 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1041 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1041 precu-

sor RNA is designated SEQ ID:27416, and is provided hereinbelow with reference to the sequence listing part.

[14531] VGAM1041 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1041 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14532] An enzyme complex designated DICER COMPLEX, dices the VGAM1041 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1041 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1041 RNA is designated SEQ ID:27417, and is provided hereinbelow with reference to the se-

quence listing part.

[14533] VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14534] VGAM1041 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1041 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1041 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14535] The complementary binding of VGAM1041 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1041 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14536] It is appreciated that VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1041 host target genes. The mRNA of each one of this plurality of VGAM1041 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1041 RNA, herein designated VGAM RNA, and which when bound by VGAM1041 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1041 host target proteins.

[14537] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1041 gene, herein designated VGAM GENE, on one or more VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14538] It is yet further appreciated that a function of VGAM1041

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1041 correlate with, and may be deduced from, the identity of the host target genes which VGAM1041 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14539] Nucleotide sequences of the VGAM1041 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1041 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1041 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1041 are further described hereinbelow with reference to Table 1.

[14540] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1041 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14541] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1042 (VGAM1042) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14542] VGAM1042 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1042 was detected is described hereinabove with reference to Figs. 2–8.

[14543] VGAM1042 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 83. VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14544] VGAM1042 gene, herein designated VGAM GENE, encodes a VGAM1042 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1042 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1042 precursor RNA is designated SEQ ID:27428, and is provided

hereinbelow with reference to the sequence listing part.

[14545] VGAM1042 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1042 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14546] An enzyme complex designated DICER COMPLEX, dices the VGAM1042 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1042 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1042 RNA is designated SEQ ID:27429, and is provided hereinbelow with reference to the sequence listing part.

[14547] VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14548] VGAM1042 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1042 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1042 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14549] The complementary binding of VGAM1042 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1042 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14550] It is appreciated that VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1042 host target genes. The mRNA of each one of this plurality of VGAM1042 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1042 RNA, herein designated VGAM RNA, and which when bound by VGAM1042 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1042 host target proteins.

[14551] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1042 gene, herein designated VGAM GENE, on one or more VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14552] It is yet further appreciated that a function of VGAM1042 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 83. Specific functions, and accordingly utilities, of VGAM1042 correlate with, and may be deduced from, the identity of the host target genes which VGAM1042 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14553] Nucleotide sequences of the VGAM1042 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1042 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1042 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1042 are further described hereinbelow with reference to Table 1.

[14554] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1042 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14555] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1043 (VGAM1043) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14556] VGAM1043 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1043 was detected is described hereinabove with reference to Figs. 2–8.

[14557] VGAM1043 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 83. VGAM1043 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14558] VGAM1043 gene, herein designated VGAM GENE, encodes a VGAM1043 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1043 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1043 precursor RNA is designated SEQ ID:27434, and is provided hereinbelow with reference to the sequence listing part.

[14559] VGAM1043 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1043 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14560] An enzyme complex designated DICER COMPLEX, dices the VGAM1043 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1043 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1043 RNA is designated SEQ ID:27435, and is provided hereinbelow with reference to the sequence listing part.

[14561] VGAM1043 host target gene, herein designated VGAM



HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14562] VGAM1043 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1043 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14563] The complementary binding of VGAM1043 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1043 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14564] It is appreciated that VGAM1043 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1043 host target genes. The mRNA of each one of this plurality of VGAM1043 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1043 RNA, herein designated VGAM

RNA, and which when bound by VGAM1043 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1043 host target proteins.

[14565] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1043 gene, herein designated VGAM GENE, on one or more VGAM1043 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14566] It is yet further appreciated that a function of VGAM1043 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1043 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 83. Specific functions, and accordingly utilities, of VGAM1043 correlate with, and may be deduced from, the identity of the host target genes which VGAM1043 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14567] Nucleotide sequences of the VGAM1043 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1043 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1043 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1043 are further described hereinbelow with reference to Table 1.

[14568] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1043 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14569] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1044 (VGAM1044) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14570] VGAM1044 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1044 was detected is described hereinabove with reference to Figs. 2-8.

[14571] VGAM1044 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14572] VGAM1044 gene, herein designated VGAM GENE, encodes a VGAM1044 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1044 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1044 precursor RNA is designated SEQ ID:27500, and is provided hereinbelow with reference to the sequence listing part.

[14573] VGAM1044 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1044 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14574] An enzyme complex designated DICER COMPLEX, dices the VGAM1044 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1044 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1044 RNA is designated SEQ ID:27501, and is provided hereinbelow with reference to the sequence listing part.

[14575] VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14576] VGAM1044 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1044 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1044 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14577] The complementary binding of VGAM1044 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1044 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14578] It is appreciated that VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1044 host target genes. The mRNA of each one of this plurality of VGAM1044 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1044 RNA, herein designated VGAM RNA, and which when bound by VGAM1044 RNA, herein



designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1044 host target proteins.

[14579] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1044 gene, herein designated VGAM GENE, on one or more VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14580] It is yet further appreciated that a function of VGAM1044 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1044 include diagnosis, prevention and

treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1044 correlate with, and may be deduced from, the identity of the host target genes which VGAM1044 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14581] Nucleotide sequences of the VGAM1044 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1044 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1044 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1044 are further described hereinbelow with reference to Table 1.

[14582] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1044 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14583] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1045 (VGAM1045) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14584] VGAM1045 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1045 was detected is described hereinabove with reference to Figs. 2–8.

[14585] VGAM1045 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1045 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14586] VGAM1045 gene, herein designated VGAM GENE, encodes a VGAM1045 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1045 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1045 precursor RNA is designated SEQ ID:27506, and is provided hereinbelow with reference to the sequence listing part.

[14587] VGAM1045 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1045 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14588] An enzyme complex designated DICER COMPLEX, dices the VGAM1045 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1045 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1045 RNA is designated SEQ ID:27507, and is provided hereinbelow with reference to the sequence listing part.

[14589] VGAM1045 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1045 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14590] VGAM1045 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1045 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14591] The complementary binding of VGAM1045 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1045 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14592] It is appreciated that VGAM1045 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1045 host target genes. The mRNA of each one of this plurality of VGAM1045 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1045 RNA, herein designated VGAM RNA, and which when bound by VGAM1045 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1045 host target proteins.

[14593] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1045 gene, herein designated VGAM GENE, on one or more VGAM1045 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14594] It is yet further appreciated that a function of VGAM1045 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific

functions, and accordingly utilities, of VGAM1045 correlate with, and may be deduced from, the identity of the host target genes which VGAM1045 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14595] Nucleotide sequences of the VGAM1045 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1045 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1045 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1045 are further described hereinbelow with reference to Table 1.

[14596] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1045 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14597] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1046 (VGAM1046) viral gene, which modulates expression of respective host target genes thereof, the func-



tion and utility of which host target genes is known in the art.

[14598] VGAM1046 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1046 was detected is described hereinabove with reference to Figs. 2–8.

[14599] VGAM1046 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Encephalomyocarditis virus. VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14600] VGAM1046 gene, herein designated VGAM GENE, encodes a VGAM1046 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1046 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1046 precursor RNA is designated SEQ ID:27523, and is provided hereinbelow with reference to the sequence listing part.

[14601] VGAM1046 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1046 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14602] An enzyme complex designated DICER COMPLEX, dices the VGAM1046 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1046 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1046 RNA is designated SEQ ID:27524, and is provided hereinbelow with reference to the sequence listing part.

[14603] VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1046 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14604] VGAM1046 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1046 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1046 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14605] The complementary binding of VGAM1046 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1046 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14606] It is appreciated that VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1046 host target genes. The mRNA of each one of this plurality of VGAM1046 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1046 RNA, herein designated VGAM RNA, and which when bound by VGAM1046 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1046 host target proteins.

[14607] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1046 gene, herein designated VGAM GENE, on one or more VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14608] It is yet further appreciated that a function of VGAM1046 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1046 include diagnosis, prevention and treatment of viral infection by Encephalomyocarditis virus. Specific functions, and accordingly utilities, of VGAM1046

correlate with, and may be deduced from, the identity of the host target genes which VGAM1046 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14609] Nucleotide sequences of the VGAM1046 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1046 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1046 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1046 are further described hereinbelow with reference to Table 1.

[14610] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1046 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14611] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1047 (VGAM1047) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[14612] VGAM1047 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1047 was detected is described hereinabove with reference to Figs. 2–8.

[14613] VGAM1047 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14614] VGAM1047 gene, herein designated VGAM GENE, encodes a VGAM1047 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1047 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1047 precursor RNA is designated SEQ ID:27575, and is provided hereinbelow with reference to the sequence listing part.

[14615] VGAM1047 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1047 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14616] An enzyme complex designated DICER COMPLEX, dices the VGAM1047 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1047 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1047 RNA is designated SEQ ID:27576, and is provided hereinbelow with reference to the sequence listing part.

[14617] VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA, comprises



three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14618] VGAM1047 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1047 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1047 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14619] The complementary binding of VGAM1047 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1047 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14620] It is appreciated that VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1047 host target genes. The mRNA of each one of this plurality of VGAM1047 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1047 RNA, herein designated VGAM RNA, and which when bound by VGAM1047 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1047 host target proteins.

[14621] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1047 gene, herein designated VGAM GENE, on one or more VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14622] It is yet further appreciated that a function of VGAM1047 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1047 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1047 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1047 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14623] Nucleotide sequences of the VGAM1047 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1047 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1047 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1047 are further described hereinbelow with reference to Table 1.

[14624] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1047 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14625] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1048 (VGAM1048) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14626] VGAM1048 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1048 was detected is described hereinabove with reference to Figs. 2–8.

[14627] VGAM1048 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14628] VGAM1048 gene, herein designated VGAM GENE, encodes a VGAM1048 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1048 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1048 precursor RNA is designated SEQ ID:27640, and is provided hereinbelow with reference to the sequence listing part.

[14629] VGAM1048 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1048 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14630] An enzyme complex designated DICER COMPLEX, dices the VGAM1048 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1048 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1048 RNA is designated SEQ ID:7182, and is provided hereinbelow with reference to the sequence listing part.

[14631] VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14632] VGAM1048 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1048 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14633] The complementary binding of VGAM1048 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1048 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14634] It is appreciated that VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1048 host target genes. The mRNA of each one of this plurality of VGAM1048 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1048 RNA, herein designated VGAM RNA, and which when bound by VGAM1048 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1048 host target proteins.

[14635] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM1048 gene, herein designated VGAM GENE, on one or more VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14636] It is yet further appreciated that a function of VGAM1048 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1048 correlate with, and may be deduced from, the identity of the host target genes which VGAM1048 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[14637] Nucleotide sequences of the VGAM1048 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1048 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1048 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1048 are further described hereinbelow with reference to Table 1.

[14638] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1048 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14639] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1049 (VGAM1049) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14640] VGAM1049 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1049 was detected is described hereinabove with reference to Figs. 2–8.

[14641] VGAM1049 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus.

VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14642] VGAM1049 gene, herein designated VGAM GENE, encodes a VGAM1049 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1049 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1049 precursor RNA is designated SEQ ID:27641, and is provided hereinbelow with reference to the sequence listing part.

[14643] VGAM1049 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1049 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14644] An enzyme complex designated DICER COMPLEX, dices the VGAM1049 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1049 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1049 RNA is designated SEQ ID:7182, and is provided hereinbelow with reference to the sequence listing part.

[14645] VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14646] VGAM1049 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1049 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1049 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3'UTR and 5'UTR regions.

[14647] The complementary binding of VGAM1049 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1049 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14648] It is appreciated that VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1049 host target genes. The mRNA of each one of this plurality of VGAM1049 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1049 RNA, herein designated VGAM RNA, and which when bound by VGAM1049 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1049 host target proteins.

[14649] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1049 gene, herein designated VGAM GENE, on one or more VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14650] It is yet further appreciated that a function of VGAM1049 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1049 correlate with, and may be deduced from, the identity of the host target genes which VGAM1049 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[14651] Nucleotide sequences of the VGAM1049 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1049 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1049 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1049 are further described hereinbelow with reference to Table 1.

[14652] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1049 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14653] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1050 (VGAM1050) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14654] VGAM1050 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.



The method by which VGAM1050 was detected is described hereinabove with reference to Figs. 2–8.

[14655] VGAM1050 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus.

VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14656] VGAM1050 gene, herein designated VGAM GENE, encodes a VGAM1050 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1050 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1050 precursor RNA is designated SEQ ID:27642, and is provided hereinbelow with reference to the sequence listing part.

[14657] VGAM1050 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1050 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14658] An enzyme complex designated DICER COMPLEX, dices the VGAM1050 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1050 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1050 RNA is designated SEQ ID:27643, and is provided hereinbelow with reference to the sequence listing part.

[14659] VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[14660] VGAM1050 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1050 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14661] The complementary binding of VGAM1050 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1050 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14662] It is appreciated that VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1050 host target genes. The mRNA of each one of this plurality of VGAM1050 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1050 RNA, herein designated VGAM RNA, and which when bound by VGAM1050 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1050 host target proteins.

[14663] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1050 gene, herein designated VGAM GENE, on one

or more VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14664] It is yet further appreciated that a function of VGAM1050 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1050 correlate with, and may be deduced from, the identity of the host target genes which VGAM1050 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14665] Nucleotide sequences of the VGAM1050 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1050 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1050 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1050 are further described hereinbelow with reference to Table 1.

[14666] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1050 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14667] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1051 (VGAM1051) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14668] VGAM1051 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1051 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[14669] VGAM1051 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus.

VGAM1051 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14670] VGAM1051 gene, herein designated VGAM GENE, encodes a VGAM1051 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1051 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1051 precursor RNA is designated SEQ ID:27648, and is provided hereinbelow with reference to the sequence listing part.

[14671] VGAM1051 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1051 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14672] An enzyme complex designated DICER COMPLEX, dices the VGAM1051 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1051 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1051 RNA is designated SEQ ID:27643, and is provided hereinbelow with reference to the sequence listing part.

[14673] VGAM1051 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.



[14674] VGAM1051 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1051 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1051 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14675] The complementary binding of VGAM1051 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1051 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14676] It is appreciated that VGAM1051 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1051 host target genes. The mRNA of each one of this plurality of VGAM1051 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1051 RNA, herein designated VGAM RNA, and which when bound by VGAM1051 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1051 host target proteins.

[14677] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1051 gene, herein designated VGAM GENE, on one or more VGAM1051 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14678] It is yet further appreciated that a function of VGAM1051 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1051 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1051 correlate with, and may be deduced from, the identity of the host target genes which VGAM1051 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14679] Nucleotide sequences of the VGAM1051 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1051 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1051 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1051 are further described hereinbelow with reference to Table 1.

[14680] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1051 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14681] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1052 (VGAM1052) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14682] VGAM1052 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1052 was detected is described hereinabove with reference to Figs. 2-8.

[14683] VGAM1052 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus.

VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14684] VGAM1052 gene, herein designated VGAM GENE, encodes a VGAM1052 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1052 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1052 precursor RNA is designated SEQ ID:27649, and is provided hereinbelow with reference to the sequence listing part.

[14685] VGAM1052 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1052 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[14686] An enzyme complex designated DICER COMPLEX, dices the VGAM1052 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1052 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1052 RNA is designated SEQ ID:27650, and is provided hereinbelow with reference to the sequence listing part.

[14687] VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14688] VGAM1052 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1052 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14689] The complementary binding of VGAM1052 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1052 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14690] It is appreciated that VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1052 host target genes. The mRNA of each one of this plurality of VGAM1052 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1052 RNA, herein designated VGAM RNA, and which when bound by VGAM1052 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1052 host target proteins.

[14691] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1052 gene, herein designated VGAM GENE, on one or more VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14692] It is yet further appreciated that a function of VGAM1052 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM1052 correlate with, and may be deduced from, the identity of the host target genes which VGAM1052 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14693] Nucleotide sequences of the VGAM1052 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1052 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1052 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1052 are further described hereinbelow with reference to Table 1.

[14694] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1052 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14695] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1053 (VGAM1053) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14696] VGAM1053 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1053 was detected is described hereinabove with reference to Figs. 2-8.

[14697] VGAM1053 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine herpesvirus 1. VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14698] VGAM1053 gene, herein designated VGAM GENE, encodes a VGAM1053 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1053 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1053 precursor RNA is designated SEQ ID:27664, and is provided hereinbelow with reference to the sequence listing part.

[14699] VGAM1053 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1053 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14700] An enzyme complex designated DICER COMPLEX, dices the VGAM1053 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1053 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1053 RNA is designated SEQ ID:27665, and is provided hereinbelow with reference to the sequence listing part.

[14701] VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14702] VGAM1053 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1053 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1053 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14703] The complementary binding of VGAM1053 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1053 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1053 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14704] It is appreciated that VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1053 host target genes. The mRNA of each one of this plurality of VGAM1053 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1053 RNA, herein designated VGAM RNA, and which when bound by VGAM1053 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1053 host target proteins.

[14705] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1053 gene, herein designated VGAM GENE, on one or more VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14706] It is yet further appreciated that a function of VGAM1053 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1053 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1053 correlate with, and may be deduced from, the identity of the host target genes which VGAM1053 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14707] Nucleotide sequences of the VGAM1053 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1053 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1053 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1053 are further described hereinbelow with reference to Table 1.

[14708] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1053 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14709] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1054 (VGAM1054) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14710] VGAM1054 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1054 was detected is described hereinabove with reference to Figs. 2-8.

[14711] VGAM1054 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5.



VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14712] VGAM1054 gene, herein designated VGAM GENE, encodes a VGAM1054 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1054 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1054 precursor RNA is designated SEQ ID:27765, and is provided hereinbelow with reference to the sequence listing part.

[14713] VGAM1054 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1054 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14714] An enzyme complex designated DICER COMPLEX, dices

the VGAM1054 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1054 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1054 RNA is designated SEQ ID:27766, and is provided hereinbelow with reference to the sequence listing part.

[14715] VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14716] VGAM1054 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1054 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1054 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1054 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14717] The complementary binding of VGAM1054 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1054 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14718] It is appreciated that VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1054 host target genes. The mRNA of each one of this plurality of VGAM1054 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1054 RNA, herein designated VGAM RNA, and which when bound by VGAM1054 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1054 host target proteins.

[14719] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1054 gene, herein designated VGAM GENE, on one or more VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14720] It is yet further appreciated that a function of VGAM1054 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1054 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1054 correlate with, and may be deduced from, the identity of the host target genes which VGAM1054 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14721] Nucleotide sequences of the VGAM1054 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1054 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1054 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1054 are further described hereinbelow with reference to Table 1.

[14722] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1054 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14723] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1055 (VGAM1055) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14724] VGAM1055 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1055 was detected is described hereinabove with reference to Figs. 2-8.

[14725] VGAM1055 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1055 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[14726] VGAM1055 gene, herein designated VGAM GENE, encodes a VGAM1055 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1055 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1055 precursor RNA is designated SEQ ID:27852, and is provided hereinbelow with reference to the sequence listing part.

[14727] VGAM1055 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1055 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14728] An enzyme complex designated DICER COMPLEX, dices the VGAM1055 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1055 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1055 RNA is designated SEQ ID:27853, and is provided hereinbelow with reference to the sequence listing part.

[14729] VGAM1055 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14730] VGAM1055 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM1055 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1055 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14731] The complementary binding of VGAM1055 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1055

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1055 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14732] It is appreciated that VGAM1055 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1055 host target genes. The mRNA of each one of this plurality of VGAM1055 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1055 RNA, herein designated VGAM RNA, and which when bound by VGAM1055 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1055 host target proteins.

[14733] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1055 gene, herein designated VGAM GENE, on one or more VGAM1055 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14734] It is yet further appreciated that a function of VGAM1055 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1055 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1055 correlate with, and may be deduced from, the identity of the host target genes which VGAM1055 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14735] Nucleotide sequences of the VGAM1055 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1055 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1055 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1055 are further described hereinbelow with reference to Table 1.

[14736] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1055 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14737] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1056 (VGAM1056) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14738] VGAM1056 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1056 was detected is described hereinabove with reference to Figs. 2-8.

[14739] VGAM1056 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[14740] VGAM1056 gene, herein designated VGAM GENE, encodes a VGAM1056 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1056 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1056 precursor RNA is designated SEQ ID:27857, and is provided hereinbelow with reference to the sequence listing part.

[14741] VGAM1056 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1056 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14742] An enzyme complex designated DICER COMPLEX, dices the VGAM1056 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1056 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1056 RNA is designated SEQ ID:27858, and is provided hereinbelow with reference to the sequence listing part.

[14743] VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14744] VGAM1056 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1056 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1056 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14745] The complementary binding of VGAM1056 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1056 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1056 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14746] It is appreciated that VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1056 host target genes. The mRNA of each one of this plurality of VGAM1056 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1056 RNA, herein designated VGAM RNA, and which when bound by VGAM1056 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1056 host target proteins.

[14747] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1056 gene, herein designated VGAM GENE, on one or more VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14748] It is yet further appreciated that a function of VGAM1056 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1056 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1056 correlate with, and may be deduced from, the identity of the host target genes which VGAM1056 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14749] Nucleotide sequences of the VGAM1056 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1056 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1056 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1056 are further

described hereinbelow with reference to Table 1.

[14750] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1056 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14751] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1057 (VGAM1057) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14752] VGAM1057 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1057 was detected is described hereinabove with reference to Figs. 2-8.

[14753] VGAM1057 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14754] VGAM1057 gene, herein designated VGAM GENE, encodes a VGAM1057 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1057 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1057 precursor RNA is designated SEQ ID:27870, and is provided hereinbelow with reference to the sequence listing part.

[14755] VGAM1057 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1057 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14756] An enzyme complex designated DICER COMPLEX, dices the VGAM1057 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1057 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1057 RNA is designated SEQ ID:27871, and is provided hereinbelow with reference to the sequence listing part.

[14757] VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14758] VGAM1057 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1057 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1057 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14759] The complementary binding of VGAM1057 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1057 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14760] It is appreciated that VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1057 host target genes. The mRNA of each one of this plurality of VGAM1057 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1057 RNA, herein designated VGAM RNA, and which when bound by VGAM1057 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1057 host target proteins.

[14761] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1057 gene, herein designated VGAM GENE, on one or more VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14762] It is yet further appreciated that a function of VGAM1057 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1057 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1057 correlate with, and may be deduced from, the identity of the host target genes which VGAM1057 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14763] Nucleotide sequences of the VGAM1057 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1057 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1057 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1057 are further described hereinbelow with reference to Table 1.

[14764] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1057 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14765] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1058 (VGAM1058) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14766] VGAM1058 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1058 was detected is described hereinabove with reference to Figs. 2-8.

[14767] VGAM1058 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14768] VGAM1058 gene, herein designated VGAM GENE, encodes



a VGAM1058 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1058 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1058 precursor RNA is designated SEQ ID:27895, and is provided hereinbelow with reference to the sequence listing part.

[14769] VGAM1058 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1058 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14770] An enzyme complex designated DICER COMPLEX, dices the VGAM1058 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1058 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1058 RNA is designated SEQ ID:27896, and is provided hereinbelow with reference to the sequence listing part.

[14771] VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14772] VGAM1058 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1058 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14773] The complementary binding of VGAM1058 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1058 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[14774] It is appreciated that VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1058 host target genes. The mRNA of each one of this plurality of VGAM1058 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1058 RNA, herein designated VGAM RNA, and which when bound by VGAM1058 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1058 host target proteins.

[14775] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1058 gene, herein designated VGAM GENE, on one or more VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14776] It is yet further appreciated that a function of VGAM1058 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1058 correlate with, and may be deduced from, the identity of the host target genes which VGAM1058 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14777] Nucleotide sequences of the VGAM1058 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1058 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1058 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1058 are further described hereinbelow with reference to Table 1.

[14778] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1058 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14779] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1059 (VGAM1059) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14780] VGAM1059 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1059 was detected is described hereinabove with reference to Figs. 2-8.

[14781] VGAM1059 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14782] VGAM1059 gene, herein designated VGAM GENE, encodes a VGAM1059 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1059 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1059 precursor RNA is designated SEQ ID:27907, and is provided hereinbelow with reference to the sequence listing part.

[14783] VGAM1059 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1059 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14784] An enzyme complex designated DICER COMPLEX, dices the VGAM1059 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1059 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1059 RNA is designated SEQ ID:27908, and is provided hereinbelow with reference to the sequence listing part.

[14785] VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14786] VGAM1059 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host



target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1059 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14787] The complementary binding of VGAM1059 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1059 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14788] It is appreciated that VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1059 host target genes. The mRNA of each one of this plurality of VGAM1059 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1059 RNA, herein designated VGAM RNA, and which when bound by VGAM1059 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1059 host target proteins.

[14789] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1059 gene, herein designated VGAM GENE, on one or more VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14790] It is yet further appreciated that a function of VGAM1059 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1059 correlate with, and may be deduced from, the identity of the host target genes which VGAM1059 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14791] Nucleotide sequences of the VGAM1059 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1059 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1059 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1059 are further described hereinbelow with reference to Table 1.

[14792] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1059 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14793] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1060 (VGAM1060) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14794] VGAM1060 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1060 was detected is described hereinabove with reference to Figs. 2-8.

[14795] VGAM1060 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1060 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14796] VGAM1060 gene, herein designated VGAM GENE, encodes a VGAM1060 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1060 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1060 precursor RNA is designated SEQ ID:27941, and is provided hereinbelow with reference to the sequence listing part.

[14797] VGAM1060 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1060 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14798] An enzyme complex designated DICER COMPLEX, dices the VGAM1060 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1060 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1060 RNA is designated SEQ ID:27942, and is provided hereinbelow with reference to the sequence listing part.

[14799] VGAM1060 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14800] VGAM1060 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1060 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14801] The complementary binding of VGAM1060 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1060 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14802] It is appreciated that VGAM1060 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1060 host target genes. The mRNA of each one of this plurality of VGAM1060 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1060 RNA, herein designated VGAM RNA, and which when bound by VGAM1060 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1060 host target proteins.

[14803] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1060 gene, herein designated VGAM GENE, on one or more VGAM1060 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14804] It is yet further appreciated that a function of VGAM1060 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1060 correlate with, and may be deduced from, the identity of the host target genes which VGAM1060 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14805] Nucleotide sequences of the VGAM1060 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1060 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1060 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1060 are further described hereinbelow with reference to Table 1.

[14806] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1060 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14807] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1061 (VGAM1061) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14808] VGAM1061 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1061 was detected is described hereinabove with reference to Figs. 2–8.

[14809] VGAM1061 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1061 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14810] VGAM1061 gene, herein designated VGAM GENE, encodes a VGAM1061 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1061 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1061 precursor RNA is designated SEQ ID:27952, and is provided hereinbelow with reference to the sequence listing part.

[14811] VGAM1061 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1061 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14812] An enzyme complex designated DICER COMPLEX, dices the VGAM1061 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1061 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1061 RNA is designated SEQ ID:27953, and is provided hereinbelow with reference to the sequence listing part.

[14813] VGAM1061 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14814] VGAM1061 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1061 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14815] The complementary binding of VGAM1061 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1061 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14816] It is appreciated that VGAM1061 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1061 host target genes. The mRNA of each one of this plurality of VGAM1061 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1061 RNA, herein designated VGAM RNA, and which when bound by VGAM1061 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1061 host target proteins.

[14817] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1061 gene, herein designated VGAM GENE, on one or more VGAM1061 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [14818] It is yet further appreciated that a function of VGAM1061 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1061 correlate with, and may be deduced from, the identity of the host target genes which VGAM1061 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [14819] Nucleotide sequences of the VGAM1061 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1061 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1061 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1061 are further described hereinbelow with reference to Table 1.
- [14820] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1061 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14821] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1062 (VGAM1062) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14822] VGAM1062 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1062 was detected is described hereinabove with reference to Figs. 2–8.

[14823] VGAM1062 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14824] VGAM1062 gene, herein designated VGAM GENE, encodes a VGAM1062 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1062 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-



code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1062 precursor RNA is designated SEQ ID:27967, and is provided hereinbelow with reference to the sequence listing part.

[14825] VGAM1062 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1062 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14826] An enzyme complex designated DICER COMPLEX, dices the VGAM1062 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1062 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM1062 RNA is designated SEQ ID:27968, and is provided hereinbelow with reference to the sequence listing part.

[14827] VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14828] VGAM1062 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1062 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1062 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14829] The complementary binding of VGAM1062 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1062 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14830] It is appreciated that VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1062 host target genes. The mRNA of

each one of this plurality of VGAM1062 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1062 RNA, herein designated VGAM RNA, and which when bound by VGAM1062 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1062 host target proteins.

[14831] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1062 gene, herein designated VGAM GENE, on one or more VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[14832] It is yet further appreciated that a function of VGAM1062 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1062 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1062 correlate with, and may be deduced from, the identity of the host target genes which VGAM1062 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14833] Nucleotide sequences of the VGAM1062 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1062 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1062 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1062 are further described hereinbelow with reference to Table 1.

[14834] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1062 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[14835] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1063 (VGAM1063) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14836] VGAM1063 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1063 was detected is described hereinabove with reference to Figs. 2–8.

[14837] VGAM1063 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 89. VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14838] VGAM1063 gene, herein designated VGAM GENE, encodes a VGAM1063 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1063 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1063 precursor RNA is designated SEQ ID:27970, and is provided hereinbelow with reference to the sequence listing part.

[14839] VGAM1063 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1063 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14840] An enzyme complex designated DICER COMPLEX, dices the VGAM1063 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1063 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1063 RNA is designated SEQ ID:27971,

and is provided hereinbelow with reference to the sequence listing part.

[14841] VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14842] VGAM1063 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1063 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14843] The complementary binding of VGAM1063 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1063 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14844] It is appreciated that VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1063 host target genes. The mRNA of each one of this plurality of VGAM1063 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1063 RNA, herein designated VGAM RNA, and which when bound by VGAM1063 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1063 host target proteins.

[14845] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1063 gene, herein designated VGAM GENE, on one or more VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14846] It is yet further appreciated that a function of VGAM1063 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 89. Specific functions, and accordingly utilities, of VGAM1063 correlate with, and may be deduced from, the identity of the host target genes which VGAM1063 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14847] Nucleotide sequences of the VGAM1063 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1063 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1063 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1063 are further described hereinbelow with reference to Table 1.

[14848] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1063 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14849] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1064 (VGAM1064) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14850] VGAM1064 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1064 was detected is described hereinabove with reference to Figs. 2–8.

[14851] VGAM1064 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 89. VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14852] VGAM1064 gene, herein designated VGAM GENE, encodes a VGAM1064 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1064 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1064 precu-

sor RNA is designated SEQ ID:27981, and is provided hereinbelow with reference to the sequence listing part.

[14853] VGAM1064 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1064 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14854] An enzyme complex designated DICER COMPLEX, dices the VGAM1064 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1064 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1064 RNA is designated SEQ ID:27982, and is provided hereinbelow with reference to the se-

quence listing part.

[14855] VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14856] VGAM1064 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1064 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14857] The complementary binding of VGAM1064 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1064 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14858] It is appreciated that VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1064 host target genes. The mRNA of each one of this plurality of VGAM1064 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1064 RNA, herein designated VGAM RNA, and which when bound by VGAM1064 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1064 host target proteins.

[14859] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1064 gene, herein designated VGAM GENE, on one or more VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14860] It is yet further appreciated that a function of VGAM1064



is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 89. Specific functions, and accordingly utilities, of VGAM1064 correlate with, and may be deduced from, the identity of the host target genes which VGAM1064 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14861] Nucleotide sequences of the VGAM1064 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1064 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1064 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1064 are further described hereinbelow with reference to Table 1.

[14862] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1064 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14863] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1065 (VGAM1065) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14864] VGAM1065 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1065 was detected is described hereinabove with reference to Figs. 2–8.

[14865] VGAM1065 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 89. VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14866] VGAM1065 gene, herein designated VGAM GENE, encodes a VGAM1065 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1065 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1065 precursor RNA is designated SEQ ID:27990, and is provided

hereinbelow with reference to the sequence listing part.

[14867] VGAM1065 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1065 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14868] An enzyme complex designated DICER COMPLEX, dices the VGAM1065 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1065 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1065 RNA is designated SEQ ID:27991, and is provided hereinbelow with reference to the sequence listing part.

[14869] VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14870] VGAM1065 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1065 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1065 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14871] The complementary binding of VGAM1065 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1065 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14872] It is appreciated that VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1065 host target genes. The mRNA of each one of this plurality of VGAM1065 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1065 RNA, herein designated VGAM RNA, and which when bound by VGAM1065 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1065 host target proteins.

[14873] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1065 gene, herein designated VGAM GENE, on one or more VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14874] It is yet further appreciated that a function of VGAM1065 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1065 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 89. Specific functions, and accordingly utilities, of VGAM1065 correlate with, and may be deduced from, the identity of the host target genes which VGAM1065 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14875] Nucleotide sequences of the VGAM1065 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1065 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1065 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1065 are further described hereinbelow with reference to Table 1.

[14876] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1065 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14877] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1066 (VGAM1066) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14878] VGAM1066 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1066 was detected is described hereinabove with reference to Figs. 2–8.

[14879] VGAM1066 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A. VGAM1066 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14880] VGAM1066 gene, herein designated VGAM GENE, encodes a VGAM1066 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1066 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1066 precursor RNA is designated SEQ ID:28004, and is provided hereinbelow with reference to the sequence listing part.



[14881] VGAM1066 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1066 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14882] An enzyme complex designated DICER COMPLEX, dices the VGAM1066 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1066 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1066 RNA is designated SEQ ID:28005, and is provided hereinbelow with reference to the sequence listing part.

[14883] VGAM1066 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14884] VGAM1066 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1066 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1066 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14885] The complementary binding of VGAM1066 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1066 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14886] It is appreciated that VGAM1066 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1066 host target genes. The mRNA of each one of this plurality of VGAM1066 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1066 RNA, herein designated VGAM

RNA, and which when bound by VGAM1066 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1066 host target proteins.

[14887] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1066 gene, herein designated VGAM GENE, on one or more VGAM1066 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14888] It is yet further appreciated that a function of VGAM1066 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1066 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM1066 correlate with, and may be deduced from, the identity of the host target genes which VGAM1066 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14889] Nucleotide sequences of the VGAM1066 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1066 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1066 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1066 are further described hereinbelow with reference to Table 1.

[14890] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1066 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14891] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1067 (VGAM1067) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14892] VGAM1067 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1067 was detected is described hereinabove with reference to Figs. 2-8.

[14893] VGAM1067 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1067 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14894] VGAM1067 gene, herein designated VGAM GENE, encodes a VGAM1067 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1067 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1067 precursor RNA is designated SEQ ID:28031, and is provided hereinbelow with reference to the sequence listing part.

[14895] VGAM1067 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1067 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14896] An enzyme complex designated DICER COMPLEX, dices the VGAM1067 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1067 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1067 RNA is designated SEQ ID:28032, and is provided hereinbelow with reference to the sequence listing part.

[14897] VGAM1067 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14898] VGAM1067 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1067 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1067 host



target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14899] The complementary binding of VGAM1067 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1067 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14900] It is appreciated that VGAM1067 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1067 host target genes. The mRNA of each one of this plurality of VGAM1067 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1067 RNA, herein designated VGAM RNA, and which when bound by VGAM1067 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1067 host target proteins.

[14901] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1067 gene, herein designated VGAM GENE, on one or more VGAM1067 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14902] It is yet further appreciated that a function of VGAM1067 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1067 include diagnosis, prevention and

treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1067 correlate with, and may be deduced from, the identity of the host target genes which VGAM1067 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14903] Nucleotide sequences of the VGAM1067 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1067 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1067 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1067 are further described hereinbelow with reference to Table 1.

[14904] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1067 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14905] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1068 (VGAM1068) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14906] VGAM1068 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1068 was detected is described hereinabove with reference to Figs. 2–8.

[14907] VGAM1068 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14908] VGAM1068 gene, herein designated VGAM GENE, encodes a VGAM1068 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1068 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1068 precursor RNA is designated SEQ ID:28035, and is provided hereinbelow with reference to the sequence listing part.

[14909] VGAM1068 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1068 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14910] An enzyme complex designated DICER COMPLEX, dices the VGAM1068 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1068 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1068 RNA is designated SEQ ID:28036, and is provided hereinbelow with reference to the sequence listing part.

[14911] VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1068 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14912] VGAM1068 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1068 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14913] The complementary binding of VGAM1068 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1068 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14914] It is appreciated that VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1068 host target genes. The mRNA of each one of this plurality of VGAM1068 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1068 RNA, herein designated VGAM RNA, and which when bound by VGAM1068 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1068 host target proteins.

[14915] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1068 gene, herein designated VGAM GENE, on one or more VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14916] It is yet further appreciated that a function of VGAM1068 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* en-



tomopoxvirus. Specific functions, and accordingly utilities, of VGAM1068 correlate with, and may be deduced from, the identity of the host target genes which VGAM1068 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14917] Nucleotide sequences of the VGAM1068 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1068 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1068 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1068 are further described hereinbelow with reference to Table 1.

[14918] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1068 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14919] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1069 (VGAM1069) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[14920] VGAM1069 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1069 was detected is described hereinabove with reference to Figs. 2–8.

[14921] VGAM1069 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Southern cowpea mosaic virus. VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14922] VGAM1069 gene, herein designated VGAM GENE, encodes a VGAM1069 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1069 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1069 precursor RNA is designated SEQ ID:28042, and is provided hereinbelow with reference to the sequence listing part.

[14923] VGAM1069 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1069 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14924] An enzyme complex designated DICER COMPLEX, dices the VGAM1069 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1069 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1069 RNA is designated SEQ ID:28043, and is provided hereinbelow with reference to the sequence listing part.

[14925] VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1069 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14926] VGAM1069 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1069 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14927] The complementary binding of VGAM1069 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1069 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14928] It is appreciated that VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1069 host target genes. The mRNA of each one of this plurality of VGAM1069 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1069 RNA, herein designated VGAM RNA, and which when bound by VGAM1069 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1069 host target proteins.

[14929] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1069 gene, herein designated VGAM GENE, on one or more VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14930] It is yet further appreciated that a function of VGAM1069 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of viral infection by Southern cowpea mosaic virus. Specific functions, and accordingly utilities, of

VGAM1069 correlate with, and may be deduced from, the identity of the host target genes which VGAM1069 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14931] Nucleotide sequences of the VGAM1069 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1069 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1069 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1069 are further described hereinbelow with reference to Table 1.

[14932] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1069 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14933] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1070 (VGAM1070) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[14934] VGAM1070 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1070 was detected is described hereinabove with reference to Figs. 2–8.

[14935] VGAM1070 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14936] VGAM1070 gene, herein designated VGAM GENE, encodes a VGAM1070 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1070 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1070 precursor RNA is designated SEQ ID:28047, and is provided hereinbelow with reference to the sequence listing part.

[14937] VGAM1070 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1070 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.



As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14938] An enzyme complex designated DICER COMPLEX, dices the VGAM1070 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1070 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1070 RNA is designated SEQ ID:28048, and is provided hereinbelow with reference to the sequence listing part.

[14939] VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14940] VGAM1070 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1070 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14941] The complementary binding of VGAM1070 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1070 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14942] It is appreciated that VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1070 host target genes. The mRNA of each one of this plurality of VGAM1070 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1070 RNA, herein designated VGAM RNA, and which when bound by VGAM1070 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1070 host target proteins.

[14943] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1070 gene, herein designated VGAM GENE, on one or more VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14944] It is yet further appreciated that a function of VGAM1070 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of viral infection by *Melanoplus sanguinipes* entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1070 correlate with, and may be deduced from,

the identity of the host target genes which VGAM1070 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14945] Nucleotide sequences of the VGAM1070 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1070 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1070 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1070 are further described hereinbelow with reference to Table 1.

[14946] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1070 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14947] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1071 (VGAM1071) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14948] VGAM1071 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1071 was detected is described hereinabove with reference to Figs. 2–8.

[14949] VGAM1071 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14950] VGAM1071 gene, herein designated VGAM GENE, encodes a VGAM1071 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1071 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1071 precursor RNA is designated SEQ ID:28050, and is provided hereinbelow with reference to the sequence listing part.

[14951] VGAM1071 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1071 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14952] An enzyme complex designated DICER COMPLEX, dices the VGAM1071 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1071 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1071 RNA is designated SEQ ID:28051, and is provided hereinbelow with reference to the sequence listing part.

[14953] VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14954] VGAM1071 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1071 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1071 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-



cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14955] The complementary binding of VGAM1071 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1071 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14956] It is appreciated that VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1071 host target genes. The mRNA of each one of this plurality of VGAM1071 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1071 RNA, herein designated VGAM RNA, and which when bound by VGAM1071 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1071 host target proteins.

[14957] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1071 gene, herein designated VGAM GENE, on one or more VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14958] It is yet further appreciated that a function of VGAM1071 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1071 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM1071 correlate with, and may be deduced from, the identity of the host target genes which VGAM1071 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[14959] Nucleotide sequences of the VGAM1071 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1071 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1071 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1071 are further described hereinbelow with reference to Table 1.

[14960] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1071 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14961] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1072 (VGAM1072) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14962] VGAM1072 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1072 was detected is described hereinabove with reference to Figs. 2–8.

[14963] VGAM1072 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1072 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14964] VGAM1072 gene, herein designated VGAM GENE, encodes a VGAM1072 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1072 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1072 precursor RNA is designated SEQ ID:28056, and is provided hereinbelow with reference to the sequence listing part.

[14965] VGAM1072 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1072 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14966] An enzyme complex designated DICER COMPLEX, dices the VGAM1072 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1072 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1072 RNA is designated SEQ ID:28057, and is provided hereinbelow with reference to the sequence listing part.

[14967] VGAM1072 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14968] VGAM1072 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1072 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1072 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[14969] The complementary binding of VGAM1072 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1072 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14970] It is appreciated that VGAM1072 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1072 host target genes. The mRNA of each one of this plurality of VGAM1072 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1072 RNA, herein designated VGAM RNA, and which when bound by VGAM1072 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1072 host target proteins.

[14971] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1072 gene, herein designated VGAM GENE, on one or more VGAM1072 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14972] It is yet further appreciated that a function of VGAM1072 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1072 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1072 correlate with, and may be deduced from, the identity of the host target genes which VGAM1072 binds and inhibits, and the function of these host target



genes, as elaborated hereinbelow.

[14973] Nucleotide sequences of the VGAM1072 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1072 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1072 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1072 are further described hereinbelow with reference to Table 1.

[14974] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1072 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14975] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1073 (VGAM1073) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14976] VGAM1073 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1073 was detected is described hereinabove with reference to Figs. 2–8.

[14977] VGAM1073 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus A. VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14978] VGAM1073 gene, herein designated VGAM GENE, encodes a VGAM1073 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1073 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1073 precursor RNA is designated SEQ ID:28068, and is provided hereinbelow with reference to the sequence listing part.

[14979] VGAM1073 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1073 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14980] An enzyme complex designated DICER COMPLEX, dices the VGAM1073 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1073 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1073 RNA is designated SEQ ID:28069, and is provided hereinbelow with reference to the sequence listing part.

[14981] VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[14982] VGAM1073 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1073 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1073 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14983] The complementary binding of VGAM1073 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1073 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14984] It is appreciated that VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1073 host target genes. The mRNA of each one of this plurality of VGAM1073 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1073 RNA, herein designated VGAM RNA, and which when bound by VGAM1073 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1073 host target proteins.

[14985] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1073 gene, herein designated VGAM GENE, on one

or more VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[14986] It is yet further appreciated that a function of VGAM1073 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1073 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus A. Specific functions, and accordingly utilities, of VGAM1073 correlate with, and may be deduced from, the identity of the host target genes which VGAM1073 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14987] Nucleotide sequences of the VGAM1073 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1073 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1073 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1073 are further described hereinbelow with reference to Table 1.

[14988] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1073 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14989] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1074 (VGAM1074) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14990] VGAM1074 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1074 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[14991] VGAM1074 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1074 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14992] VGAM1074 gene, herein designated VGAM GENE, encodes a VGAM1074 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1074 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1074 precursor RNA is designated SEQ ID:28087, and is provided hereinbelow with reference to the sequence listing part.

[14993] VGAM1074 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1074 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14994] An enzyme complex designated DICER COMPLEX, dices the VGAM1074 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1074 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1074 RNA is designated SEQ ID:28088, and is provided hereinbelow with reference to the sequence listing part.

[14995] VGAM1074 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[14996] VGAM1074 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1074 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[14997] The complementary binding of VGAM1074 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1074 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14998] It is appreciated that VGAM1074 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1074 host target genes. The mRNA of each one of this plurality of VGAM1074 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1074 RNA, herein designated VGAM RNA, and which when bound by VGAM1074 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1074 host target proteins.

[14999] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1074 gene, herein designated VGAM GENE, on one or more VGAM1074 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15000] It is yet further appreciated that a function of VGAM1074 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1074 correlate with, and may be deduced from, the identity of the host target genes which VGAM1074 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15001] Nucleotide sequences of the VGAM1074 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1074 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1074 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1074 are further described hereinbelow with reference to Table 1.

[15002] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1074 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15003] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1075 (VGAM1075) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15004] VGAM1075 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1075 was detected is described hereinabove with reference to Figs. 2-8.

[15005] VGAM1075 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15006] VGAM1075 gene, herein designated VGAM GENE, encodes a VGAM1075 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1075 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1075 precursor RNA is designated SEQ ID:28099, and is provided hereinbelow with reference to the sequence listing part.

[15007] VGAM1075 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1075 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[15008] An enzyme complex designated DICER COMPLEX, dices the VGAM1075 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1075 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1075 RNA is designated SEQ ID:28100, and is provided hereinbelow with reference to the sequence listing part.

[15009] VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15010] VGAM1075 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1075 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1075 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15011] The complementary binding of VGAM1075 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1075 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15012] It is appreciated that VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1075 host target genes. The mRNA of each one of this plurality of VGAM1075 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1075 RNA, herein designated VGAM RNA, and which when bound by VGAM1075 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1075 host target proteins.

[15013] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1075 gene, herein designated VGAM GENE, on one or more VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15014] It is yet further appreciated that a function of VGAM1075 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1075 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1075 correlate with, and may be deduced from, the identity of the host target genes which VGAM1075 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15015] Nucleotide sequences of the VGAM1075 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1075 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1075 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1075 are further described hereinbelow with reference to Table 1.

[15016] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1075 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15017] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1076 (VGAM1076) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15018] VGAM1076 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1076 was detected is described hereinabove with reference to Figs. 2-8.

[15019] VGAM1076 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Melon necrotic spot virus. VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15020] VGAM1076 gene, herein designated VGAM GENE, encodes a VGAM1076 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1076 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1076 precursor RNA is designated SEQ ID:28103, and is provided hereinbelow with reference to the sequence listing part.

[15021] VGAM1076 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1076 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15022] An enzyme complex designated DICER COMPLEX, dices the VGAM1076 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1076 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1076 RNA is designated SEQ ID:28104, and is provided hereinbelow with reference to the sequence listing part.

[15023] VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15024] VGAM1076 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1076 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15025] The complementary binding of VGAM1076 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1076 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1076 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15026] It is appreciated that VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1076 host target genes. The mRNA of each one of this plurality of VGAM1076 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1076 RNA, herein designated VGAM RNA, and which when bound by VGAM1076 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1076 host target proteins.

[15027] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1076 gene, herein designated VGAM GENE, on one or more VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15028] It is yet further appreciated that a function of VGAM1076 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of viral infection by Melon necrotic spot virus. Specific functions, and accordingly utilities, of VGAM1076 correlate with, and may be deduced from, the identity of the host target genes which VGAM1076 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15029] Nucleotide sequences of the VGAM1076 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1076 RNA, herein designated VGAM RNA, and



a schematic representation of the secondary folding of VGAM1076 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1076 are further described hereinbelow with reference to Table 1.

[15030] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1076 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15031] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1077 (VGAM1077) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15032] VGAM1077 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1077 was detected is described hereinabove with reference to Figs. 2-8.

[15033] VGAM1077 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15034] VGAM1077 gene, herein designated VGAM GENE, encodes a VGAM1077 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1077 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1077 precursor RNA is designated SEQ ID:28134, and is provided hereinbelow with reference to the sequence listing part.

[15035] VGAM1077 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1077 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15036] An enzyme complex designated DICER COMPLEX, dices

the VGAM1077 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1077 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1077 RNA is designated SEQ ID:28135, and is provided hereinbelow with reference to the sequence listing part.

[15037] VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15038] VGAM1077 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1077 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1077 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15039] The complementary binding of VGAM1077 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1077 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15040] It is appreciated that VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1077 host target genes. The mRNA of each one of this plurality of VGAM1077 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1077 RNA, herein designated VGAM RNA, and which when bound by VGAM1077 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1077 host target proteins.

[15041] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1077 gene, herein designated VGAM GENE, on one or more VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15042] It is yet further appreciated that a function of VGAM1077 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1077 correlate with, and may be deduced from, the identity of the host target genes which VGAM1077 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15043] Nucleotide sequences of the VGAM1077 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1077 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1077 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1077 are further described hereinbelow with reference to Table 1.

[15044] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1077 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15045] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1078 (VGAM1078) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15046] VGAM1078 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1078 was detected is described hereinabove with reference to Figs. 2-8.

[15047] VGAM1078 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melon necrotic spot virus. VGAM1078 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15048] VGAM1078 gene, herein designated VGAM GENE, encodes a VGAM1078 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1078 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1078 precursor RNA is designated SEQ ID:28143, and is provided hereinbelow with reference to the sequence listing part.

[15049] VGAM1078 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1078 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15050] An enzyme complex designated DICER COMPLEX, dices the VGAM1078 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM1078 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1078 RNA is designated SEQ ID:28144, and is provided hereinbelow with reference to the sequence listing part.

[15051] VGAM1078 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15052] VGAM1078 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1078 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15053] The complementary binding of VGAM1078 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1078

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1078 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15054] It is appreciated that VGAM1078 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1078 host target genes. The mRNA of each one of this plurality of VGAM1078 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1078 RNA, herein designated VGAM RNA, and which when bound by VGAM1078 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1078 host target proteins.

[15055] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1078 gene, herein designated VGAM GENE, on one or more VGAM1078 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15056] It is yet further appreciated that a function of VGAM1078 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of viral infection by Melon necrotic spot virus. Specific functions, and accordingly utilities, of VGAM1078 correlate with, and may be deduced from, the identity of the host target genes which VGAM1078 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15057] Nucleotide sequences of the VGAM1078 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1078 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1078 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1078 are further described hereinbelow with reference to Table 1.

[15058] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1078 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15059] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1079 (VGAM1079) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15060] VGAM1079 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1079 was detected is described hereinabove with reference to Figs. 2-8.

[15061] VGAM1079 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melon necrotic spot virus. VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[15062] VGAM1079 gene, herein designated VGAM GENE, encodes a VGAM1079 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1079 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1079 precursor RNA is designated SEQ ID:28153, and is provided hereinbelow with reference to the sequence listing part.

[15063] VGAM1079 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1079 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15064] An enzyme complex designated DICER COMPLEX, dices the VGAM1079 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1079 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1079 RNA is designated SEQ ID:28154, and is provided hereinbelow with reference to the sequence listing part.

[15065] VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15066] VGAM1079 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1079 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1079 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15067] The complementary binding of VGAM1079 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1079 host target RNA, herein designated VGAM HOST TARGET



RNA, into VGAM1079 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15068] It is appreciated that VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1079 host target genes. The mRNA of each one of this plurality of VGAM1079 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1079 RNA, herein designated VGAM RNA, and which when bound by VGAM1079 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1079 host target proteins.

[15069] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1079 gene, herein designated VGAM GENE, on one or more VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15070] It is yet further appreciated that a function of VGAM1079 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1079 include diagnosis, prevention and treatment of viral infection by Melon necrotic spot virus. Specific functions, and accordingly utilities, of VGAM1079 correlate with, and may be deduced from, the identity of the host target genes which VGAM1079 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15071] Nucleotide sequences of the VGAM1079 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1079 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1079 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1079 are further

described hereinbelow with reference to Table 1.

[15072] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1079 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15073] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1080 (VGAM1080) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15074] VGAM1080 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1080 was detected is described hereinabove with reference to Figs. 2-8.

[15075] VGAM1080 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15076] VGAM1080 gene, herein designated VGAM GENE, encodes a VGAM1080 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1080 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1080 precursor RNA is designated SEQ ID:28165, and is provided hereinbelow with reference to the sequence listing part.

[15077] VGAM1080 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1080 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15078] An enzyme complex designated DICER COMPLEX, dices the VGAM1080 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1080 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1080 RNA is designated SEQ ID:28166, and is provided hereinbelow with reference to the sequence listing part.

[15079] VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15080] VGAM1080 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1080 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1080 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15081] The complementary binding of VGAM1080 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1080 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15082] It is appreciated that VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1080 host target genes. The mRNA of each one of this plurality of VGAM1080 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1080 RNA, herein designated VGAM RNA, and which when bound by VGAM1080 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1080 host target proteins.

[15083] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1080 gene, herein designated VGAM GENE, on one or more VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15084] It is yet further appreciated that a function of VGAM1080 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1080 correlate with, and may be deduced from, the identity of the host target genes which VGAM1080 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15085] Nucleotide sequences of the VGAM1080 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1080 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1080 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1080 are further described hereinbelow with reference to Table 1.



[15086] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1080 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15087] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1081 (VGAM1081) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15088] VGAM1081 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1081 was detected is described hereinabove with reference to Figs. 2-8.

[15089] VGAM1081 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 70. VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15090] VGAM1081 gene, herein designated VGAM GENE, encodes

a VGAM1081 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1081 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1081 precursor RNA is designated SEQ ID:28169, and is provided hereinbelow with reference to the sequence listing part.

[15091] VGAM1081 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1081 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15092] An enzyme complex designated DICER COMPLEX, dices the VGAM1081 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1081 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1081 RNA is designated SEQ ID:28170, and is provided hereinbelow with reference to the sequence listing part.

[15093] VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15094] VGAM1081 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1081 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15095] The complementary binding of VGAM1081 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1081 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[15096] It is appreciated that VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1081 host target genes. The mRNA of each one of this plurality of VGAM1081 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1081 RNA, herein designated VGAM RNA, and which when bound by VGAM1081 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1081 host target proteins.

[15097] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1081 gene, herein designated VGAM GENE, on one or more VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15098] It is yet further appreciated that a function of VGAM1081 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 70. Specific functions, and accordingly utilities, of VGAM1081 correlate with, and may be deduced from, the identity of the host target genes which VGAM1081 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15099] Nucleotide sequences of the VGAM1081 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1081 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1081 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1081 are further described hereinbelow with reference to Table 1.

[15100] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1081 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15101] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1082 (VGAM1082) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15102] VGAM1082 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1082 was detected is described hereinabove with reference to Figs. 2-8.

[15103] VGAM1082 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15104] VGAM1082 gene, herein designated VGAM GENE, encodes a VGAM1082 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1082 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1082 precursor RNA is designated SEQ ID:28187, and is provided hereinbelow with reference to the sequence listing part.

[15105] VGAM1082 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1082 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15106] An enzyme complex designated DICER COMPLEX, dices the VGAM1082 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1082 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1082 RNA is designated SEQ ID:28188, and is provided hereinbelow with reference to the sequence listing part.

[15107] VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15108] VGAM1082 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1082 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1082 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15109] The complementary binding of VGAM1082 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1082 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15110] It is appreciated that VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1082 host target genes. The mRNA of each one of this plurality of VGAM1082 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1082 RNA, herein designated VGAM RNA, and which when bound by VGAM1082 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1082 host target proteins.

[15111] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1082 gene, herein designated VGAM GENE, on one or more VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15112] It is yet further appreciated that a function of VGAM1082 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1082 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1082 correlate with, and may be deduced from, the identity of the host target genes which VGAM1082 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15113] Nucleotide sequences of the VGAM1082 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1082 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1082 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1082 are further described hereinbelow with reference to Table 1.

[15114] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1082 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15115] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1083 (VGAM1083) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15116] VGAM1083 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1083 was detected is described hereinabove with reference to Figs. 2-8.

[15117] VGAM1083 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM1083 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15118] VGAM1083 gene, herein designated VGAM GENE, encodes a VGAM1083 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1083 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1083 precursor RNA is designated SEQ ID:28209, and is provided hereinbelow with reference to the sequence listing part.

[15119] VGAM1083 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1083 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15120] An enzyme complex designated DICER COMPLEX, dices the VGAM1083 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1083 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1083 RNA is designated SEQ ID:28210, and is provided hereinbelow with reference to the sequence listing part.

[15121] VGAM1083 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15122] VGAM1083 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1083 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15123] The complementary binding of VGAM1083 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1083 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15124] It is appreciated that VGAM1083 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1083 host target genes. The mRNA of each one of this plurality of VGAM1083 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1083 RNA, herein designated VGAM RNA, and which when bound by VGAM1083 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1083 host target proteins.

[15125] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1083 gene, herein designated VGAM GENE, on one or more VGAM1083 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15126] It is yet further appreciated that a function of VGAM1083 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1083 correlate with, and may be deduced from, the identity of the host target genes which VGAM1083 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15127] Nucleotide sequences of the VGAM1083 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1083 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1083 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1083 are further described hereinbelow with reference to Table 1.

[15128] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1083 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15129] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1084 (VGAM1084) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15130] VGAM1084 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1084 was detected is described hereinabove with reference to Figs. 2–8.

[15131] VGAM1084 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15132] VGAM1084 gene, herein designated VGAM GENE, encodes a VGAM1084 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1084 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1084 precursor RNA is designated SEQ ID:28226, and is provided hereinbelow with reference to the sequence listing part.

[15133] VGAM1084 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1084 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15134] An enzyme complex designated DICER COMPLEX, dices the VGAM1084 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1084 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1084 RNA is designated SEQ ID:28227, and is provided hereinbelow with reference to the sequence listing part.

[15135] VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15136] VGAM1084 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1084 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15137] The complementary binding of VGAM1084 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1084 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15138] It is appreciated that VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1084 host target genes. The mRNA of each one of this plurality of VGAM1084 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1084 RNA, herein designated VGAM RNA, and which when bound by VGAM1084 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1084 host target proteins.

[15139] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1084 gene, herein designated VGAM GENE, on one or more VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [15140] It is yet further appreciated that a function of VGAM1084 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of viral infection by Mollusum contagiosum virus. Specific functions, and accordingly utilities, of VGAM1084 correlate with, and may be deduced from, the identity of the host target genes which VGAM1084 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [15141] Nucleotide sequences of the VGAM1084 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1084 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1084 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1084 are further described hereinbelow with reference to Table 1.
- [15142] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM1084 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15143] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1085 (VGAM1085) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15144] VGAM1085 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1085 was detected is described hereinabove with reference to Figs. 2-8.

[15145] VGAM1085 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15146] VGAM1085 gene, herein designated VGAM GENE, encodes a VGAM1085 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1085 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1085 precursor RNA is designated SEQ ID:28254, and is provided hereinbelow with reference to the sequence listing part.

[15147] VGAM1085 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1085 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15148] An enzyme complex designated DICER COMPLEX, dices the VGAM1085 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1085 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM1085 RNA is designated SEQ ID:28255, and is provided hereinbelow with reference to the sequence listing part.

[15149] VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15150] VGAM1085 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1085 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1085 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15151] The complementary binding of VGAM1085 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1085 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15152] It is appreciated that VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1085 host target genes. The mRNA of

each one of this plurality of VGAM1085 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1085 RNA, herein designated VGAM RNA, and which when bound by VGAM1085 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1085 host target proteins.

[15153] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1085 gene, herein designated VGAM GENE, on one or more VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[15154] It is yet further appreciated that a function of VGAM1085 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1085 correlate with, and may be deduced from, the identity of the host target genes which VGAM1085 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15155] Nucleotide sequences of the VGAM1085 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1085 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1085 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1085 are further described hereinbelow with reference to Table 1.

[15156] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1085 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[15157] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1086 (VGAM1086) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15158] VGAM1086 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1086 was detected is described hereinabove with reference to Figs. 2–8.

[15159] VGAM1086 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1086 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15160] VGAM1086 gene, herein designated VGAM GENE, encodes a VGAM1086 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1086 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1086 precursor RNA is designated SEQ ID:28287, and is provided hereinbelow with reference to the sequence listing part.

[15161] VGAM1086 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1086 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15162] An enzyme complex designated DICER COMPLEX, dices the VGAM1086 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1086 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1086 RNA is designated SEQ ID:28288,



and is provided hereinbelow with reference to the sequence listing part.

[15163] VGAM1086 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1086 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1086 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15164] VGAM1086 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1086 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1086 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1086 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15165] The complementary binding of VGAM1086 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1086 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1086 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1086 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15166] It is appreciated that VGAM1086 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1086 host target genes. The mRNA of each one of this plurality of VGAM1086 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1086 RNA, herein designated VGAM RNA, and which when bound by VGAM1086 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1086 host target proteins.

[15167] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1086 gene, herein designated VGAM GENE, on one or more VGAM1086 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15168] It is yet further appreciated that a function of VGAM1086 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1086 correlate with, and may be deduced from, the identity of the host target genes which VGAM1086 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15169] Nucleotide sequences of the VGAM1086 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1086 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1086 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1086 are further described hereinbelow with reference to Table 1.

[15170] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1086 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15171] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1087 (VGAM1087) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15172] VGAM1087 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1087 was detected is described hereinabove with reference to Figs. 2–8.

[15173] VGAM1087 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15174] VGAM1087 gene, herein designated VGAM GENE, encodes a VGAM1087 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1087 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1087 precu-

sor RNA is designated SEQ ID:28300, and is provided hereinbelow with reference to the sequence listing part.

[15175] VGAM1087 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1087 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15176] An enzyme complex designated DICER COMPLEX, dices the VGAM1087 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1087 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1087 RNA is designated SEQ ID:28301, and is provided hereinbelow with reference to the se-

quence listing part.

[15177] VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15178] VGAM1087 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1087 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15179] The complementary binding of VGAM1087 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1087 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15180] It is appreciated that VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1087 host target genes. The mRNA of each one of this plurality of VGAM1087 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1087 RNA, herein designated VGAM RNA, and which when bound by VGAM1087 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1087 host target proteins.

[15181] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1087 gene, herein designated VGAM GENE, on one or more VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15182] It is yet further appreciated that a function of VGAM1087

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1087 correlate with, and may be deduced from, the identity of the host target genes which VGAM1087 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15183] Nucleotide sequences of the VGAM1087 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1087 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1087 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1087 are further described hereinbelow with reference to Table 1.

[15184] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1087 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15185] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1088 (VGAM1088) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15186] VGAM1088 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1088 was detected is described hereinabove with reference to Figs. 2–8.

[15187] VGAM1088 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15188] VGAM1088 gene, herein designated VGAM GENE, encodes a VGAM1088 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1088 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1088 precursor RNA is designated SEQ ID:28308, and is provided

hereinbelow with reference to the sequence listing part.

[15189] VGAM1088 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1088 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15190] An enzyme complex designated DICER COMPLEX, dices the VGAM1088 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1088 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1088 RNA is designated SEQ ID:28309, and is provided hereinbelow with reference to the sequence listing part.

[15191] VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15192] VGAM1088 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1088 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1088 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15193] The complementary binding of VGAM1088 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1088 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15194] It is appreciated that VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1088 host target genes. The mRNA of each one of this plurality of VGAM1088 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1088 RNA, herein designated VGAM RNA, and which when bound by VGAM1088 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1088 host target proteins.

[15195] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1088 gene, herein designated VGAM GENE, on one or more VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15196] It is yet further appreciated that a function of VGAM1088 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1088 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1088 correlate with, and may be deduced from, the identity of the host target genes which VGAM1088 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15197] Nucleotide sequences of the VGAM1088 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1088 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1088 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1088 are further described hereinbelow with reference to Table 1.

[15198] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1088 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15199] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 1089 (VGAM1089) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15200] VGAM1089 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1089 was detected is described hereinabove with reference to Figs. 2–8.

[15201] VGAM1089 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1089 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15202] VGAM1089 gene, herein designated VGAM GENE, encodes a VGAM1089 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1089 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1089 precursor RNA is designated SEQ ID:28314, and is provided hereinbelow with reference to the sequence listing part.

[15203] VGAM1089 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1089 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15204] An enzyme complex designated DICER COMPLEX, dices the VGAM1089 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1089 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1089 RNA is designated SEQ ID:28315, and is provided hereinbelow with reference to the sequence listing part.

[15205] VGAM1089 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15206] VGAM1089 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1089 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15207] The complementary binding of VGAM1089 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1089 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15208] It is appreciated that VGAM1089 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1089 host target genes. The mRNA of each one of this plurality of VGAM1089 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1089 RNA, herein designated VGAM

RNA, and which when bound by VGAM1089 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1089 host target proteins.

[15209] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1089 gene, herein designated VGAM GENE, on one or more VGAM1089 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15210] It is yet further appreciated that a function of VGAM1089 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1089 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1089 correlate with, and may be deduced from, the identity of the host target genes which VGAM1089 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15211] Nucleotide sequences of the VGAM1089 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1089 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1089 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1089 are further described hereinbelow with reference to Table 1.

[15212] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1089 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15213] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1090 (VGAM1090) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15214] VGAM1090 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1090 was detected is described hereinabove with reference to Figs. 2–8.

[15215] VGAM1090 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15216] VGAM1090 gene, herein designated VGAM GENE, encodes a VGAM1090 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1090 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1090 precursor RNA is designated SEQ ID:28319, and is provided hereinbelow with reference to the sequence listing part.

[15217] VGAM1090 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1090 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15218] An enzyme complex designated DICER COMPLEX, dices the VGAM1090 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1090 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1090 RNA is designated SEQ ID:28320, and is provided hereinbelow with reference to the sequence listing part.

[15219] VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15220] VGAM1090 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1090 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1090 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15221] The complementary binding of VGAM1090 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1090 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15222] It is appreciated that VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1090 host target genes. The mRNA of each one of this plurality of VGAM1090 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1090 RNA, herein designated VGAM RNA, and which when bound by VGAM1090 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1090 host target proteins.

[15223] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1090 gene, herein designated VGAM GENE, on one or more VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15224] It is yet further appreciated that a function of VGAM1090 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1090 include diagnosis, prevention and

treatment of viral infection by Saimiriine herpesvirus 2.

Specific functions, and accordingly utilities, of VGAM1090 correlate with, and may be deduced from, the identity of the host target genes which VGAM1090 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15225] Nucleotide sequences of the VGAM1090 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1090 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1090 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1090 are further described hereinbelow with reference to Table 1.

[15226] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1090 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15227] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1091 (VGAM1091) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15228] VGAM1091 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1091 was detected is described hereinabove with reference to Figs. 2–8.

[15229] VGAM1091 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15230] VGAM1091 gene, herein designated VGAM GENE, encodes a VGAM1091 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1091 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1091 precursor RNA is designated SEQ ID:28341, and is provided hereinbelow with reference to the sequence listing part.

[15231] VGAM1091 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1091 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15232] An enzyme complex designated DICER COMPLEX, dices the VGAM1091 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1091 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1091 RNA is designated SEQ ID:28342, and is provided hereinbelow with reference to the sequence listing part.

[15233] VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1091 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15234] VGAM1091 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1091 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1091 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15235] The complementary binding of VGAM1091 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1091 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15236] It is appreciated that VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1091 host target genes. The mRNA of each one of this plurality of VGAM1091 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1091 RNA, herein designated VGAM RNA, and which when bound by VGAM1091 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM1091 host target proteins.

[15237] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1091 gene, herein designated VGAM GENE, on one or more VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15238] It is yet further appreciated that a function of VGAM1091 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1091 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific

functions, and accordingly utilities, of VGAM1091 correlate with, and may be deduced from, the identity of the host target genes which VGAM1091 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15239] Nucleotide sequences of the VGAM1091 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1091 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1091 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1091 are further described hereinbelow with reference to Table 1.

[15240] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1091 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15241] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1092 (VGAM1092) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[15242] VGAM1092 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1092 was detected is described hereinabove with reference to Figs. 2–8.

[15243] VGAM1092 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Satellite tobacco mosaic virus. VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15244] VGAM1092 gene, herein designated VGAM GENE, encodes a VGAM1092 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1092 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1092 precursor RNA is designated SEQ ID:28351, and is provided hereinbelow with reference to the sequence listing part.

[15245] VGAM1092 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1092 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15246] An enzyme complex designated DICER COMPLEX, dices the VGAM1092 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1092 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1092 RNA is designated SEQ ID:28352, and is provided hereinbelow with reference to the sequence listing part.

[15247] VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1092 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15248] VGAM1092 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1092 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1092 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15249] The complementary binding of VGAM1092 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1092 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15250] It is appreciated that VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1092 host target genes. The mRNA of each one of this plurality of VGAM1092 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1092 RNA, herein designated VGAM RNA, and which when bound by VGAM1092 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1092 host target proteins.

[15251] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1092 gene, herein designated VGAM GENE, on one or more VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15252] It is yet further appreciated that a function of VGAM1092 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1092 include diagnosis, prevention and treatment of viral infection by Satellite tobacco mosaic virus. Specific functions, and accordingly utilities, of

VGAM1092 correlate with, and may be deduced from, the identity of the host target genes which VGAM1092 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15253] Nucleotide sequences of the VGAM1092 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1092 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1092 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1092 are further described hereinbelow with reference to Table 1.

[15254] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1092 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15255] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1093 (VGAM1093) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[15256] VGAM1093 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1093 was detected is described hereinabove with reference to Figs. 2–8.

[15257] VGAM1093 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15258] VGAM1093 gene, herein designated VGAM GENE, encodes a VGAM1093 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1093 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1093 precursor RNA is designated SEQ ID:28369, and is provided hereinbelow with reference to the sequence listing part.

[15259] VGAM1093 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1093 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15260] An enzyme complex designated DICER COMPLEX, dices the VGAM1093 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1093 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1093 RNA is designated SEQ ID:28370, and is provided hereinbelow with reference to the sequence listing part.

[15261] VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15262] VGAM1093 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1093 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15263] The complementary binding of VGAM1093 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1093 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15264] It is appreciated that VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1093 host target genes. The mRNA of each one of this plurality of VGAM1093 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1093 RNA, herein designated VGAM RNA, and which when bound by VGAM1093 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1093 host target proteins.

[15265] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1093 gene, herein designated VGAM GENE, on one or more VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15266] It is yet further appreciated that a function of VGAM1093 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1093 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1093 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15267] Nucleotide sequences of the VGAM1093 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1093 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1093 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1093 are further described hereinbelow with reference to Table 1.

[15268] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1093 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15269] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1094 (VGAM1094) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15270] VGAM1094 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1094 was detected is described hereinabove with reference to Figs. 2–8.

[15271] VGAM1094 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15272] VGAM1094 gene, herein designated VGAM GENE, encodes a VGAM1094 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1094 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1094 precursor RNA is designated SEQ ID:28382, and is provided hereinbelow with reference to the sequence listing part.

[15273] VGAM1094 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1094 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15274] An enzyme complex designated DICER COMPLEX, dices the VGAM1094 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1094 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1094 RNA is designated SEQ ID:28383, and is provided hereinbelow with reference to the sequence listing part.

[15275] VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding



gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15276] VGAM1094 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1094 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1094 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15277] The complementary binding of VGAM1094 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1094 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15278] It is appreciated that VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1094 host target genes. The mRNA of each one of this plurality of VGAM1094 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1094 RNA, herein designated VGAM RNA, and which when bound by VGAM1094 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1094 host target proteins.

[15279] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1094 gene, herein designated VGAM GENE, on one or more VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15280] It is yet further appreciated that a function of VGAM1094 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1094 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1094 correlate with, and may be deduced from, the identity of the host target genes which VGAM1094 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[15281] Nucleotide sequences of the VGAM1094 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1094 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1094 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1094 are further described hereinbelow with reference to Table 1.

[15282] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1094 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15283] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1095 (VGAM1095) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15284] VGAM1095 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1095 was detected is described hereinabove with reference to Figs. 2–8.

[15285] VGAM1095 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus.

VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15286] VGAM1095 gene, herein designated VGAM GENE, encodes a VGAM1095 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1095 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1095 precursor RNA is designated SEQ ID:28419, and is provided hereinbelow with reference to the sequence listing part.

[15287] VGAM1095 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1095 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15288] An enzyme complex designated DICER COMPLEX, dices the VGAM1095 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1095 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1095 RNA is designated SEQ ID:28420, and is provided hereinbelow with reference to the sequence listing part.

[15289] VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15290] VGAM1095 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1095 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1095 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[15291] The complementary binding of VGAM1095 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1095 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15292] It is appreciated that VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1095 host target genes. The mRNA of each one of this plurality of VGAM1095 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1095 RNA, herein designated VGAM RNA, and which when bound by VGAM1095 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1095 host target proteins.

[15293] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM1095 gene, herein designated VGAM GENE, on one or more VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15294] It is yet further appreciated that a function of VGAM1095 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1095 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1095 correlate with, and may be deduced from, the identity of the host target genes which VGAM1095 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[15295] Nucleotide sequences of the VGAM1095 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1095 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1095 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1095 are further described hereinbelow with reference to Table 1.

[15296] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1095 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15297] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1096 (VGAM1096) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15298] VGAM1096 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1096 was detected is described hereinabove with reference to Figs. 2–8.

[15299] VGAM1096 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM1096 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15300] VGAM1096 gene, herein designated VGAM GENE, encodes a VGAM1096 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1096 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1096 precursor RNA is designated SEQ ID:28431, and is provided hereinbelow with reference to the sequence listing part.

[15301] VGAM1096 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1096 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15302] An enzyme complex designated DICER COMPLEX, dices the VGAM1096 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1096 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1096 RNA is designated SEQ ID:28432, and is provided hereinbelow with reference to the sequence listing part.

[15303] VGAM1096 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[15304] VGAM1096 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1096 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15305] The complementary binding of VGAM1096 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1096 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15306] It is appreciated that VGAM1096 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1096 host target genes. The mRNA of each one of this plurality of VGAM1096 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1096 RNA, herein designated VGAM RNA, and which when bound by VGAM1096 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1096 host target proteins.

[15307] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1096 gene, herein designated VGAM GENE, on one or more VGAM1096 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15308] It is yet further appreciated that a function of VGAM1096 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1096 correlate with, and may be deduced from, the identity of the host target genes which VGAM1096 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15309] Nucleotide sequences of the VGAM1096 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM1096 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1096 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1096 are further described hereinbelow with reference to Table 1.

[15310] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1096 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15311] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1097 (VGAM1097) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15312] VGAM1097 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1097 was detected is described hereinabove with reference to Figs. 2-8.

[15313] VGAM1097 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15314] VGAM1097 gene, herein designated VGAM GENE, encodes a VGAM1097 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1097 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1097 precursor RNA is designated SEQ ID:28501, and is provided hereinbelow with reference to the sequence listing part.

[15315] VGAM1097 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1097 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[15316] An enzyme complex designated DICER COMPLEX, dices the VGAM1097 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1097 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1097 RNA is designated SEQ ID:28502, and is provided hereinbelow with reference to the sequence listing part.

[15317] VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15318] VGAM1097 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1097 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1097 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15319] The complementary binding of VGAM1097 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1097 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15320] It is appreciated that VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1097 host target genes. The mRNA of each one of this plurality of VGAM1097 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1097 RNA, herein designated VGAM RNA, and which when bound by VGAM1097 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1097 host target proteins.

[15321] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1097 gene, herein designated VGAM GENE, on one or more VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15322] It is yet further appreciated that a function of VGAM1097 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1097 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1097 correlate with, and may be deduced from, the identity of the host target genes which VGAM1097 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15323] Nucleotide sequences of the VGAM1097 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1097 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1097 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1097 are further described hereinbelow with reference to Table 1.

[15324] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1097 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15325] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1098 (VGAM1098) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15326] VGAM1098 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1098 was detected is described hereinabove with reference to Figs. 2-8.

[15327] VGAM1098 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine herpesvirus 2. VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15328] VGAM1098 gene, herein designated VGAM GENE, encodes a VGAM1098 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1098 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1098 precursor RNA is designated SEQ ID:28522, and is provided hereinbelow with reference to the sequence listing part.

[15329] VGAM1098 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1098 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[15330] An enzyme complex designated DICER COMPLEX, dices the VGAM1098 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1098 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1098 RNA is designated SEQ ID:28523, and is provided hereinbelow with reference to the sequence listing part.

[15331] VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15332] VGAM1098 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1098 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15333] The complementary binding of VGAM1098 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1098 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1098 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15334] It is appreciated that VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1098 host target genes. The mRNA of each one of this plurality of VGAM1098 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1098 RNA, herein designated VGAM RNA, and which when bound by VGAM1098 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1098 host target proteins.

[15335] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1098 gene, herein designated VGAM GENE, on one or more VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15336] It is yet further appreciated that a function of VGAM1098 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1098 correlate with, and may be deduced from, the identity of the host target genes which VGAM1098 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15337] Nucleotide sequences of the VGAM1098 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1098 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1098 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1098 are further described hereinbelow with reference to Table 1.

[15338] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1098 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15339] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1099 (VGAM1099) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15340] VGAM1099 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1099 was detected is described hereinabove with reference to Figs. 2-8.

[15341] VGAM1099 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola virus. VGAM1099

host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15342] VGAM1099 gene, herein designated VGAM GENE, encodes a VGAM1099 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1099 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1099 precursor RNA is designated SEQ ID:28542, and is provided hereinbelow with reference to the sequence listing part.

[15343] VGAM1099 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1099 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15344] An enzyme complex designated DICER COMPLEX, dices the VGAM1099 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1099 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1099 RNA is designated SEQ ID:28342, and is provided hereinbelow with reference to the sequence listing part.

[15345] VGAM1099 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15346] VGAM1099 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1099 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1099 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15347] The complementary binding of VGAM1099 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1099



host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1099 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15348] It is appreciated that VGAM1099 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1099 host target genes. The mRNA of each one of this plurality of VGAM1099 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1099 RNA, herein designated VGAM RNA, and which when bound by VGAM1099 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1099 host target proteins.

[15349] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1099 gene, herein designated VGAM GENE, on one or more VGAM1099 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15350] It is yet further appreciated that a function of VGAM1099 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1099 include diagnosis, prevention and treatment of viral infection by Variola virus. Specific functions, and accordingly utilities, of VGAM1099 correlate with, and may be deduced from, the identity of the host target genes which VGAM1099 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15351] Nucleotide sequences of the VGAM1099 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1099 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1099 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1099 are further described hereinbelow with reference to Table 1.

[15352] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1099 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15353] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1100 (VGAM1100) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15354] VGAM1100 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1100 was detected is described hereinabove with reference to Figs. 2-8.

[15355] VGAM1100 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[15356] VGAM1100 gene, herein designated VGAM GENE, encodes a VGAM1100 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1100 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1100 precursor RNA is designated SEQ ID:28543, and is provided hereinbelow with reference to the sequence listing part.

[15357] VGAM1100 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15358] An enzyme complex designated DICER COMPLEX, dices the VGAM1100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1100 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1100 RNA is designated SEQ ID:28544, and is provided hereinbelow with reference to the sequence listing part.

[15359] VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15360] VGAM1100 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1100 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15361] The complementary binding of VGAM1100 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1100 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1100 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15362] It is appreciated that VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1100 host target genes. The mRNA of each one of this plurality of VGAM1100 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1100 RNA, herein designated VGAM RNA, and which when bound by VGAM1100 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1100 host target proteins.

[15363] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1100 gene, herein designated VGAM GENE, on one or more VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15364] It is yet further appreciated that a function of VGAM1100 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1100 correlate with, and may be deduced from, the identity of the host target genes which VGAM1100 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15365] Nucleotide sequences of the VGAM1100 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1100 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1100 are further



described hereinbelow with reference to Table 1.

[15366] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1100 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15367] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1101 (VGAM1101) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15368] VGAM1101 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1101 was detected is described hereinabove with reference to Figs. 2-8.

[15369] VGAM1101 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 52. VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15370] VGAM1101 gene, herein designated VGAM GENE, encodes a VGAM1101 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1101 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1101 precursor RNA is designated SEQ ID:28563, and is provided hereinbelow with reference to the sequence listing part.

[15371] VGAM1101 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15372] An enzyme complex designated DICER COMPLEX, dices the VGAM1101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1101 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1101 RNA is designated SEQ ID:28564, and is provided hereinbelow with reference to the sequence listing part.

[15373] VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15374] VGAM1101 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1101 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1101 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15375] The complementary binding of VGAM1101 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1101 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15376] It is appreciated that VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1101 host target genes. The mRNA of each one of this plurality of VGAM1101 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1101 RNA, herein designated VGAM RNA, and which when bound by VGAM1101 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1101 host target proteins.

[15377] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1101 gene, herein designated VGAM GENE, on one or more VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15378] It is yet further appreciated that a function of VGAM1101 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 52. Specific functions, and accordingly utilities, of VGAM1101 correlate with, and may be deduced from, the identity of the host target genes which VGAM1101 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15379] Nucleotide sequences of the VGAM1101 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1101 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1101 are further described hereinbelow with reference to Table 1.

[15380] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1101 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15381] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1102 (VGAM1102) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15382] VGAM1102 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1102 was detected is described hereinabove with reference to Figs. 2-8.

[15383] VGAM1102 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15384] VGAM1102 gene, herein designated VGAM GENE, encodes

a VGAM1102 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1102 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1102 precursor RNA is designated SEQ ID:28577, and is provided hereinbelow with reference to the sequence listing part.

[15385] VGAM1102 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15386] An enzyme complex designated DICER COMPLEX, dices the VGAM1102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1102 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1102 RNA is designated SEQ ID:28578, and is provided hereinbelow with reference to the sequence listing part.

[15387] VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15388] VGAM1102 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1102 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1102 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15389] The complementary binding of VGAM1102 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1102 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[15390] It is appreciated that VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1102 host target genes. The mRNA of each one of this plurality of VGAM1102 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1102 RNA, herein designated VGAM RNA, and which when bound by VGAM1102 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1102 host target proteins.

[15391] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1102 gene, herein designated VGAM GENE, on one or more VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15392] It is yet further appreciated that a function of VGAM1102 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1102 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1102 correlate with, and may be deduced from, the identity of the host target genes which VGAM1102 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15393] Nucleotide sequences of the VGAM1102 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1102 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1102 are further described hereinbelow with reference to Table 1.

[15394] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1102 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15395] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1103 (VGAM1103) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15396] VGAM1103 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1103 was detected is described hereinabove with reference to Figs. 2-8.

[15397] VGAM1103 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 59. VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15398] VGAM1103 gene, herein designated VGAM GENE, encodes a VGAM1103 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1103 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1103 precursor RNA is designated SEQ ID:28582, and is provided hereinbelow with reference to the sequence listing part.

[15399] VGAM1103 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15400] An enzyme complex designated DICER COMPLEX, dices the VGAM1103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1103 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1103 RNA is designated SEQ ID:28583, and is provided hereinbelow with reference to the sequence listing part.

[15401] VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15402] VGAM1103 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1103 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15403] The complementary binding of VGAM1103 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1103 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[15404] It is appreciated that VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1103 host target genes. The mRNA of each one of this plurality of VGAM1103 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1103 RNA, herein designated VGAM RNA, and which when bound by VGAM1103 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1103 host target proteins.

[15405] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1103 gene, herein designated VGAM GENE, on one or more VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15406] It is yet further appreciated that a function of VGAM1103 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 59. Specific functions, and accordingly utilities, of VGAM1103 correlate with, and may be deduced from, the identity of the host target genes which VGAM1103 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15407] Nucleotide sequences of the VGAM1103 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1103 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1103 are further described hereinbelow with reference to Table 1.

[15408] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1103 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15409] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1104 (VGAM1104) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15410] VGAM1104 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1104 was detected is described hereinabove with reference to Figs. 2-8.

[15411] VGAM1104 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox virus. VGAM1104 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15412] VGAM1104 gene, herein designated VGAM GENE, encodes a VGAM1104 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1104 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1104 precursor RNA is designated SEQ ID:28609, and is provided hereinbelow with reference to the sequence listing part.

[15413] VGAM1104 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15414] An enzyme complex designated DICER COMPLEX, dices the VGAM1104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1104 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1104 RNA is designated SEQ ID:28610, and is provided hereinbelow with reference to the sequence listing part.

[15415] VGAM1104 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15416] VGAM1104 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1104 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1104 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15417] The complementary binding of VGAM1104 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1104 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15418] It is appreciated that VGAM1104 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1104 host target genes. The mRNA of each one of this plurality of VGAM1104 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1104 RNA, herein designated VGAM RNA, and which when bound by VGAM1104 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1104 host target proteins.

[15419] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1104 gene, herein designated VGAM GENE, on one or more VGAM1104 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15420] It is yet further appreciated that a function of VGAM1104 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1104 include diagnosis, prevention and treatment of viral infection by Monkeypox virus. Specific functions, and accordingly utilities, of VGAM1104 correlate with, and may be deduced from, the identity of the host target genes which VGAM1104 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15421] Nucleotide sequences of the VGAM1104 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1104 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1104 are further described hereinbelow with reference to Table 1.

[15422] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the



complementarity of each of these host target binding sites to VGAM1104 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15423] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1105 (VGAM1105) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15424] VGAM1105 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1105 was detected is described hereinabove with reference to Figs. 2–8.

[15425] VGAM1105 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 59. VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15426] VGAM1105 gene, herein designated VGAM GENE, encodes a VGAM1105 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1105 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1105 precursor RNA is designated SEQ ID:28615, and is provided hereinbelow with reference to the sequence listing part.

[15427] VGAM1105 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15428] An enzyme complex designated DICER COMPLEX, dices the VGAM1105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1105 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1105 RNA is designated SEQ ID:28616, and is provided hereinbelow with reference to the sequence listing part.

[15429] VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15430] VGAM1105 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1105 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15431] The complementary binding of VGAM1105 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1105 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15432] It is appreciated that VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1105 host target genes. The mRNA of each one of this plurality of VGAM1105 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1105 RNA, herein designated VGAM RNA, and which when bound by VGAM1105 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1105 host target proteins.

[15433] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1105 gene, herein designated VGAM GENE, on one or more VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [15434] It is yet further appreciated that a function of VGAM1105 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 59. Specific functions, and accordingly utilities, of VGAM1105 correlate with, and may be deduced from, the identity of the host target genes which VGAM1105 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [15435] Nucleotide sequences of the VGAM1105 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1105 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1105 are further described hereinbelow with reference to Table 1.
- [15436] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1105 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15437] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1106 (VGAM1106) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15438] VGAM1106 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1106 was detected is described hereinabove with reference to Figs. 2-8.

[15439] VGAM1106 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 59. VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15440] VGAM1106 gene, herein designated VGAM GENE, encodes a VGAM1106 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1106 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1106 precursor RNA is designated SEQ ID:28676, and is provided hereinbelow with reference to the sequence listing part.

[15441] VGAM1106 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15442] An enzyme complex designated DICER COMPLEX, dices the VGAM1106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1106 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-



quence of VGAM1106 RNA is designated SEQ ID:28677, and is provided hereinbelow with reference to the sequence listing part.

[15443] VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15444] VGAM1106 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1106 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1106 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15445] The complementary binding of VGAM1106 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1106 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15446] It is appreciated that VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1106 host target genes. The mRNA of

each one of this plurality of VGAM1106 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1106 RNA, herein designated VGAM RNA, and which when bound by VGAM1106 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1106 host target proteins.

[15447] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1106 gene, herein designated VGAM GENE, on one or more VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[15448] It is yet further appreciated that a function of VGAM1106 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1106 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 59. Specific functions, and accordingly utilities, of VGAM1106 correlate with, and may be deduced from, the identity of the host target genes which VGAM1106 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15449] Nucleotide sequences of the VGAM1106 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1106 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1106 are further described hereinbelow with reference to Table 1.

[15450] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1106 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[15451] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1107 (VGAM1107) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15452] VGAM1107 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1107 was detected is described hereinabove with reference to Figs. 2–8.

[15453] VGAM1107 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15454] VGAM1107 gene, herein designated VGAM GENE, encodes a VGAM1107 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1107 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1107 precursor RNA is designated SEQ ID:28714, and is provided hereinbelow with reference to the sequence listing part.

[15455] VGAM1107 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15456] An enzyme complex designated DICER COMPLEX, dices the VGAM1107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1107 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1107 RNA is designated SEQ ID:28715,

and is provided hereinbelow with reference to the sequence listing part.

[15457] VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15458] VGAM1107 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1107 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15459] The complementary binding of VGAM1107 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1107 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15460] It is appreciated that VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1107 host target genes. The mRNA of each one of this plurality of VGAM1107 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1107 RNA, herein designated VGAM RNA, and which when bound by VGAM1107 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1107 host target proteins.

[15461] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1107 gene, herein designated VGAM GENE, on one or more VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15462] It is yet further appreciated that a function of VGAM1107 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1107 correlate with, and may be deduced from, the identity of the host target genes which VGAM1107 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15463] Nucleotide sequences of the VGAM1107 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1107 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1107 are further described hereinbelow with reference to Table 1.

[15464] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1107 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15465] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1108 (VGAM1108) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15466] VGAM1108 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1108 was detected is described hereinabove with reference to Figs. 2–8.

[15467] VGAM1108 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15468] VGAM1108 gene, herein designated VGAM GENE, encodes a VGAM1108 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1108 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1108 precu-

sor RNA is designated SEQ ID:28724, and is provided hereinbelow with reference to the sequence listing part.

[15469] VGAM1108 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15470] An enzyme complex designated DICER COMPLEX, dices the VGAM1108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1108 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1108 RNA is designated SEQ ID:28725, and is provided hereinbelow with reference to the se-

quence listing part.

[15471] VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15472] VGAM1108 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1108 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1108 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15473] The complementary binding of VGAM1108 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1108 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15474] It is appreciated that VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1108 host target genes. The mRNA of each one of this plurality of VGAM1108 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1108 RNA, herein designated VGAM RNA, and which when bound by VGAM1108 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1108 host target proteins.

[15475] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1108 gene, herein designated VGAM GENE, on one or more VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15476] It is yet further appreciated that a function of VGAM1108

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1108 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1108 correlate with, and may be deduced from, the identity of the host target genes which VGAM1108 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15477] Nucleotide sequences of the VGAM1108 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1108 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1108 are further described hereinbelow with reference to Table 1.

[15478] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1108 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15479] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1109 (VGAM1109) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15480] VGAM1109 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1109 was detected is described hereinabove with reference to Figs. 2–8.

[15481] VGAM1109 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15482] VGAM1109 gene, herein designated VGAM GENE, encodes a VGAM1109 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1109 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1109 precursor RNA is designated SEQ ID:28758, and is provided

hereinbelow with reference to the sequence listing part.

[15483] VGAM1109 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15484] An enzyme complex designated DICER COMPLEX, dices the VGAM1109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1109 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1109 RNA is designated SEQ ID:28759, and is provided hereinbelow with reference to the sequence listing part.

[15485] VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15486] VGAM1109 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1109 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1109 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15487] The complementary binding of VGAM1109 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1109 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15488] It is appreciated that VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1109 host target genes. The mRNA of each one of this plurality of VGAM1109 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1109 RNA, herein designated VGAM RNA, and which when bound by VGAM1109 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1109 host target proteins.

[15489] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1109 gene, herein designated VGAM GENE, on one or more VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15490] It is yet further appreciated that a function of VGAM1109 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1109 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1109 correlate with, and may be deduced from, the identity of the host target genes which VGAM1109 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15491] Nucleotide sequences of the VGAM1109 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1109 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1109 are further described hereinbelow with reference to Table 1.

[15492] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1109 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15493] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1110 (VGAM1110) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15494] VGAM1110 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1110 was detected is described hereinabove with reference to Figs. 2–8.

[15495] VGAM1110 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like disease virus. VGAM1110 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15496] VGAM1110 gene, herein designated VGAM GENE, encodes a VGAM1110 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1110 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1110 precursor RNA is designated SEQ ID:28764, and is provided hereinbelow with reference to the sequence listing part.

[15497] VGAM1110 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15498] An enzyme complex designated DICER COMPLEX, dices the VGAM1110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1110 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1110 RNA is designated SEQ ID:28765, and is provided hereinbelow with reference to the sequence listing part.

[15499] VGAM1110 host target gene, herein designated VGAM



HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15500] VGAM1110 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1110 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1110 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15501] The complementary binding of VGAM1110 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1110 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15502] It is appreciated that VGAM1110 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1110 host target genes. The mRNA of each one of this plurality of VGAM1110 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1110 RNA, herein designated VGAM

RNA, and which when bound by VGAM1110 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1110 host target proteins.

[15503] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1110 gene, herein designated VGAM GENE, on one or more VGAM1110 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15504] It is yet further appreciated that a function of VGAM1110 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1110 include diagnosis, prevention and treatment of viral infection by Yaba-like disease virus. Specific functions, and accordingly utilities, of VGAM1110 correlate with, and may be deduced from, the identity of the host target genes which VGAM1110 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15505] Nucleotide sequences of the VGAM1110 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1110 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1110 are further described hereinbelow with reference to Table 1.

[15506] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1110 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15507] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1111 (VGAM1111) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15508] VGAM1111 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1111 was detected is described hereinabove with reference to Figs. 2-8.

[15509] VGAM1111 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 51. VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15510] VGAM1111 gene, herein designated VGAM GENE, encodes a VGAM1111 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1111 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1111 precursor RNA is designated SEQ ID:28776, and is provided hereinbelow with reference to the sequence listing part.

[15511] VGAM1111 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15512] An enzyme complex designated DICER COMPLEX, dices the VGAM1111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1111 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1111 RNA is designated SEQ ID:28777, and is provided hereinbelow with reference to the sequence listing part.

[15513] VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15514] VGAM1111 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1111 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1111 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15515] The complementary binding of VGAM1111 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1111 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15516] It is appreciated that VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1111 host target genes. The mRNA of each one of this plurality of VGAM1111 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1111 RNA, herein designated VGAM RNA, and which when bound by VGAM1111 RNA, herein



designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1111 host target proteins.

[15517] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1111 gene, herein designated VGAM GENE, on one or more VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15518] It is yet further appreciated that a function of VGAM1111 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1111 include diagnosis, prevention and

treatment of viral infection by Human papillomavirus type 51. Specific functions, and accordingly utilities, of VGAM1111 correlate with, and may be deduced from, the identity of the host target genes which VGAM1111 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15519] Nucleotide sequences of the VGAM1111 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1111 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1111 are further described hereinbelow with reference to Table 1.

[15520] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1111 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15521] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1112 (VGAM1112) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15522] VGAM1112 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1112 was detected is described hereinabove with reference to Figs. 2–8.

[15523] VGAM1112 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15524] VGAM1112 gene, herein designated VGAM GENE, encodes a VGAM1112 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1112 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1112 precursor RNA is designated SEQ ID:28804, and is provided hereinbelow with reference to the sequence listing part.

[15525] VGAM1112 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1112 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15526] An enzyme complex designated DICER COMPLEX, dices the VGAM1112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1112 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1112 RNA is designated SEQ ID:28805, and is provided hereinbelow with reference to the sequence listing part.

[15527] VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1112 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15528] VGAM1112 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1112 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1112 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15529] The complementary binding of VGAM1112 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1112 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15530] It is appreciated that VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1112 host target genes. The mRNA of each one of this plurality of VGAM1112 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1112 RNA, herein designated VGAM RNA, and which when bound by VGAM1112 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1112 host target proteins.

[15531] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1112 gene, herein designated VGAM GENE, on one or more VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15532] It is yet further appreciated that a function of VGAM1112 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1112 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific

functions, and accordingly utilities, of VGAM1112 correlate with, and may be deduced from, the identity of the host target genes which VGAM1112 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15533] Nucleotide sequences of the VGAM1112 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1112 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1112 are further described hereinbelow with reference to Table 1.

[15534] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1112 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15535] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1113 (VGAM1113) viral gene, which modulates expression of respective host target genes thereof, the func-



tion and utility of which host target genes is known in the art.

[15536] VGAM1113 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1113 was detected is described hereinabove with reference to Figs. 2–8.

[15537] VGAM1113 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 51. VGAM1113 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15538] VGAM1113 gene, herein designated VGAM GENE, encodes a VGAM1113 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1113 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1113 precursor RNA is designated SEQ ID:28819, and is provided hereinbelow with reference to the sequence listing part.

[15539] VGAM1113 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1113 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15540] An enzyme complex designated DICER COMPLEX, dices the VGAM1113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1113 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1113 RNA is designated SEQ ID:28820, and is provided hereinbelow with reference to the sequence listing part.

[15541] VGAM1113 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1113 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15542] VGAM1113 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1113 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15543] The complementary binding of VGAM1113 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1113 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15544] It is appreciated that VGAM1113 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1113 host target genes. The mRNA of each one of this plurality of VGAM1113 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1113 RNA, herein designated VGAM RNA, and which when bound by VGAM1113 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1113 host target proteins.

[15545] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1113 gene, herein designated VGAM GENE, on one or more VGAM1113 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15546] It is yet further appreciated that a function of VGAM1113 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 51. Specific functions, and accordingly utilities, of

VGAM1113 correlate with, and may be deduced from, the identity of the host target genes which VGAM1113 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15547] Nucleotide sequences of the VGAM1113 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1113 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1113 are further described hereinbelow with reference to Table 1.

[15548] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1113 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15549] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1114 (VGAM1114) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[15550] VGAM1114 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1114 was detected is described hereinabove with reference to Figs. 2–8.

[15551] VGAM1114 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15552] VGAM1114 gene, herein designated VGAM GENE, encodes a VGAM1114 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1114 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1114 precursor RNA is designated SEQ ID:28834, and is provided hereinbelow with reference to the sequence listing part.

[15553] VGAM1114 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15554] An enzyme complex designated DICER COMPLEX, dices the VGAM1114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1114 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1114 RNA is designated SEQ ID:28835, and is provided hereinbelow with reference to the sequence listing part.

[15555] VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA, comprises



three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15556] VGAM1114 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1114 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15557] The complementary binding of VGAM1114 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1114 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15558] It is appreciated that VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1114 host target genes. The mRNA of each one of this plurality of VGAM1114 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1114 RNA, herein designated VGAM RNA, and which when bound by VGAM1114 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1114 host target proteins.

[15559] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1114 gene, herein designated VGAM GENE, on one or more VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15560] It is yet further appreciated that a function of VGAM1114 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1114 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1114 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15561] Nucleotide sequences of the VGAM1114 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1114 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1114 are further described hereinbelow with reference to Table 1.

[15562] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1114 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15563] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1115 (VGAM1115) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15564] VGAM1115 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1115 was detected is described hereinabove with reference to Figs. 2–8.

[15565] VGAM1115 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15566] VGAM1115 gene, herein designated VGAM GENE, encodes a VGAM1115 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1115 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1115 precursor RNA is designated SEQ ID:28864, and is provided hereinbelow with reference to the sequence listing part.

[15567] VGAM1115 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15568] An enzyme complex designated DICER COMPLEX, dices the VGAM1115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1115 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1115 RNA is designated SEQ ID:28865, and is provided hereinbelow with reference to the sequence listing part.

[15569] VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15570] VGAM1115 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1115 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15571] The complementary binding of VGAM1115 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1115 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15572] It is appreciated that VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1115 host target genes. The mRNA of each one of this plurality of VGAM1115 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1115 RNA, herein designated VGAM RNA, and which when bound by VGAM1115 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1115 host target proteins.

[15573] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM1115 gene, herein designated VGAM GENE, on one or more VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15574] It is yet further appreciated that a function of VGAM1115 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1115 correlate with, and may be deduced from, the identity of the host target genes which VGAM1115 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[15575] Nucleotide sequences of the VGAM1115 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1115 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1115 are further described hereinbelow with reference to Table 1.

[15576] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1115 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15577] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1116 (VGAM1116) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15578] VGAM1116 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1116 was detected is described hereinabove with reference to Figs. 2–8.

[15579] VGAM1116 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 84. VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15580] VGAM1116 gene, herein designated VGAM GENE, encodes a VGAM1116 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1116 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1116 precursor RNA is designated SEQ ID:28878, and is provided hereinbelow with reference to the sequence listing part.

[15581] VGAM1116 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15582] An enzyme complex designated DICER COMPLEX, dices the VGAM1116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1116 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1116 RNA is designated SEQ ID:28879, and is provided hereinbelow with reference to the sequence listing part.

[15583] VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15584] VGAM1116 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1116 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1116 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[15585] The complementary binding of VGAM1116 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1116 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15586] It is appreciated that VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1116 host target genes. The mRNA of each one of this plurality of VGAM1116 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1116 RNA, herein designated VGAM RNA, and which when bound by VGAM1116 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1116 host target proteins.

[15587] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1116 gene, herein designated VGAM GENE, on one or more VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15588] It is yet further appreciated that a function of VGAM1116 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1116 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 84. Specific functions, and accordingly utilities, of VGAM1116 correlate with, and may be deduced from, the identity of the host target genes which VGAM1116 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[15589] Nucleotide sequences of the VGAM1116 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1116 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1116 are further described hereinbelow with reference to Table 1.

[15590] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1116 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15591] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1117 (VGAM1117) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15592] VGAM1117 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.



The method by which VGAM1117 was detected is described hereinabove with reference to Figs. 2–8.

[15593] VGAM1117 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine enterovirus.

VGAM1117 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15594] VGAM1117 gene, herein designated VGAM GENE, encodes a VGAM1117 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1117 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1117 precursor RNA is designated SEQ ID:28885, and is provided hereinbelow with reference to the sequence listing part.

[15595] VGAM1117 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15596] An enzyme complex designated DICER COMPLEX, dices the VGAM1117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1117 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1117 RNA is designated SEQ ID:28886, and is provided hereinbelow with reference to the sequence listing part.

[15597] VGAM1117 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[15598] VGAM1117 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1117 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1117 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15599] The complementary binding of VGAM1117 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1117 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15600] It is appreciated that VGAM1117 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1117 host target genes. The mRNA of each one of this plurality of VGAM1117 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1117 RNA, herein designated VGAM RNA, and which when bound by VGAM1117 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1117 host target proteins.

[15601] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1117 gene, herein designated VGAM GENE, on one

or more VGAM1117 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15602] It is yet further appreciated that a function of VGAM1117 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1117 include diagnosis, prevention and treatment of viral infection by Bovine enterovirus. Specific functions, and accordingly utilities, of VGAM1117 correlate with, and may be deduced from, the identity of the host target genes which VGAM1117 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15603] Nucleotide sequences of the VGAM1117 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1117 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1117 are further described hereinbelow with reference to Table 1.

[15604] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1117 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15605] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1118 (VGAM1118) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15606] VGAM1118 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1118 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[15607] VGAM1118 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine enterovirus.

VGAM1118 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15608] VGAM1118 gene, herein designated VGAM GENE, encodes a VGAM1118 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1118 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1118 precursor RNA is designated SEQ ID:28917, and is provided hereinbelow with reference to the sequence listing part.

[15609] VGAM1118 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15610] An enzyme complex designated DICER COMPLEX, dices the VGAM1118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1118 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1118 RNA is designated SEQ ID:28918, and is provided hereinbelow with reference to the sequence listing part.

[15611] VGAM1118 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.



[15612] VGAM1118 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1118 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1118 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15613] The complementary binding of VGAM1118 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1118 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15614] It is appreciated that VGAM1118 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1118 host target genes. The mRNA of each one of this plurality of VGAM1118 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1118 RNA, herein designated VGAM RNA, and which when bound by VGAM1118 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1118 host target proteins.

[15615] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1118 gene, herein designated VGAM GENE, on one or more VGAM1118 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15616] It is yet further appreciated that a function of VGAM1118 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1118 include diagnosis, prevention and treatment of viral infection by Bovine enterovirus. Specific functions, and accordingly utilities, of VGAM1118 correlate with, and may be deduced from, the identity of the host target genes which VGAM1118 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15617] Nucleotide sequences of the VGAM1118 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1118 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1118 are further described hereinbelow with reference to Table 1.

[15618] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1118 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15619] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1119 (VGAM1119) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15620] VGAM1119 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1119 was detected is described hereinabove with reference to Figs. 2-8.

[15621] VGAM1119 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 84. VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15622] VGAM1119 gene, herein designated VGAM GENE, encodes a VGAM1119 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1119 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1119 precursor RNA is designated SEQ ID:28955, and is provided hereinbelow with reference to the sequence listing part.

[15623] VGAM1119 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[15624] An enzyme complex designated DICER COMPLEX, dices the VGAM1119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1119 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1119 RNA is designated SEQ ID:28956, and is provided hereinbelow with reference to the sequence listing part.

[15625] VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15626] VGAM1119 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1119 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1119 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15627] The complementary binding of VGAM1119 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1119 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15628] It is appreciated that VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1119 host target genes. The mRNA of each one of this plurality of VGAM1119 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1119 RNA, herein designated VGAM RNA, and which when bound by VGAM1119 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1119 host target proteins.

[15629] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1119 gene, herein designated VGAM GENE, on one or more VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15630] It is yet further appreciated that a function of VGAM1119 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 84. Specific functions, and accordingly utilities, of VGAM1119 correlate with, and may be deduced from, the identity of the host target genes which VGAM1119 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15631] Nucleotide sequences of the VGAM1119 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1119 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1119 are further described hereinbelow with reference to Table 1.

[15632] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1119 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15633] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1120 (VGAM1120) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15634] VGAM1120 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1120 was detected is described hereinabove with reference to Figs. 2-8.

[15635] VGAM1120 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine herpesvirus 4. VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15636] VGAM1120 gene, herein designated VGAM GENE, encodes a VGAM1120 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1120 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1120 precursor RNA is designated SEQ ID:28974, and is provided hereinbelow with reference to the sequence listing part.

[15637] VGAM1120 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15638] An enzyme complex designated DICER COMPLEX, dices the VGAM1120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1120 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1120 RNA is designated SEQ ID:28975, and is provided hereinbelow with reference to the sequence listing part.

[15639] VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15640] VGAM1120 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1120 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15641] The complementary binding of VGAM1120 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1120 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1120 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15642] It is appreciated that VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1120 host target genes. The mRNA of each one of this plurality of VGAM1120 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1120 RNA, herein designated VGAM RNA, and which when bound by VGAM1120 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1120 host target proteins.

[15643] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1120 gene, herein designated VGAM GENE, on one or more VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15644] It is yet further appreciated that a function of VGAM1120 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1120 correlate with, and may be deduced from, the identity of the host target genes which VGAM1120 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15645] Nucleotide sequences of the VGAM1120 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1120 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1120 are further described hereinbelow with reference to Table 1.

[15646] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1120 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15647] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1121 (VGAM1121) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15648] VGAM1121 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1121 was detected is described hereinabove with reference to Figs. 2-8.

[15649] VGAM1121 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus C.



VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15650] VGAM1121 gene, herein designated VGAM GENE, encodes a VGAM1121 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1121 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1121 precursor RNA is designated SEQ ID:29050, and is provided hereinbelow with reference to the sequence listing part.

[15651] VGAM1121 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15652] An enzyme complex designated DICER COMPLEX, dices

the VGAM1121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1121 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1121 RNA is designated SEQ ID:29051, and is provided hereinbelow with reference to the sequence listing part.

[15653] VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15654] VGAM1121 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1121 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1121 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1121 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15655] The complementary binding of VGAM1121 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1121 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15656] It is appreciated that VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1121 host target genes. The mRNA of each one of this plurality of VGAM1121 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1121 RNA, herein designated VGAM RNA, and which when bound by VGAM1121 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1121 host target proteins.

[15657] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1121 gene, herein designated VGAM GENE, on one or more VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15658] It is yet further appreciated that a function of VGAM1121 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1121 include diagnosis, prevention and treatment of viral infection by Human adenovirus C. Specific functions, and accordingly utilities, of VGAM1121 correlate with, and may be deduced from, the identity of the host target genes which VGAM1121 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15659] Nucleotide sequences of the VGAM1121 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1121 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1121 are further described hereinbelow with reference to Table 1.

[15660] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1121 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15661] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1122 (VGAM1122) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15662] VGAM1122 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1122 was detected is described hereinabove with reference to Figs. 2-8.

[15663] VGAM1122 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1122 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[15664] VGAM1122 gene, herein designated VGAM GENE, encodes a VGAM1122 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1122 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1122 precursor RNA is designated SEQ ID:29063, and is provided hereinbelow with reference to the sequence listing part.

[15665] VGAM1122 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15666] An enzyme complex designated DICER COMPLEX, dices the VGAM1122 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1122 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1122 RNA is designated SEQ ID:29064, and is provided hereinbelow with reference to the sequence listing part.

[15667] VGAM1122 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15668] VGAM1122 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1122 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15669] The complementary binding of VGAM1122 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1122

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1122 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15670] It is appreciated that VGAM1122 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1122 host target genes. The mRNA of each one of this plurality of VGAM1122 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1122 RNA, herein designated VGAM RNA, and which when bound by VGAM1122 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1122 host target proteins.

[15671] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1122 gene, herein designated VGAM GENE, on one or more VGAM1122 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15672] It is yet further appreciated that a function of VGAM1122 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1122 correlate with, and may be deduced from, the identity of the host target genes which VGAM1122 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15673] Nucleotide sequences of the VGAM1122 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1122 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1122 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1122 are further described hereinbelow with reference to Table 1.

[15674] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1122 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15675] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1123 (VGAM1123) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15676] VGAM1123 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1123 was detected is described hereinabove with reference to Figs. 2-8.

[15677] VGAM1123 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1123 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[15678] VGAM1123 gene, herein designated VGAM GENE, encodes a VGAM1123 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1123 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1123 precursor RNA is designated SEQ ID:29069, and is provided hereinbelow with reference to the sequence listing part.

[15679] VGAM1123 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15680] An enzyme complex designated DICER COMPLEX, dices the VGAM1123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1123 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1123 RNA is designated SEQ ID:29070, and is provided hereinbelow with reference to the sequence listing part.

[15681] VGAM1123 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15682] VGAM1123 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1123 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15683] The complementary binding of VGAM1123 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1123 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1123 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15684] It is appreciated that VGAM1123 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1123 host target genes. The mRNA of each one of this plurality of VGAM1123 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1123 RNA, herein designated VGAM RNA, and which when bound by VGAM1123 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1123 host target proteins.

[15685] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1123 gene, herein designated VGAM GENE, on one or more VGAM1123 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15686] It is yet further appreciated that a function of VGAM1123 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1123 correlate with, and may be deduced from, the identity of the host target genes which VGAM1123 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15687] Nucleotide sequences of the VGAM1123 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1123 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1123 are further

described hereinbelow with reference to Table 1.

[15688] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1123 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15689] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1124 (VGAM1124) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15690] VGAM1124 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1124 was detected is described hereinabove with reference to Figs. 2-8.

[15691] VGAM1124 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15692] VGAM1124 gene, herein designated VGAM GENE, encodes a VGAM1124 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1124 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1124 precursor RNA is designated SEQ ID:29080, and is provided hereinbelow with reference to the sequence listing part.

[15693] VGAM1124 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15694] An enzyme complex designated DICER COMPLEX, dices the VGAM1124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1124 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1124 RNA is designated SEQ ID:29081, and is provided hereinbelow with reference to the sequence listing part.

[15695] VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15696] VGAM1124 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1124 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1124 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15697] The complementary binding of VGAM1124 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1124 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15698] It is appreciated that VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1124 host target genes. The mRNA of each one of this plurality of VGAM1124 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1124 RNA, herein designated VGAM RNA, and which when bound by VGAM1124 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1124 host target proteins.

[15699] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1124 gene, herein designated VGAM GENE, on one or more VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15700] It is yet further appreciated that a function of VGAM1124 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1124 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1124 correlate with, and may be deduced from, the identity of the host target genes which VGAM1124 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15701] Nucleotide sequences of the VGAM1124 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1124 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1124 are further described hereinbelow with reference to Table 1.

[15702] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1124 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15703] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1125 (VGAM1125) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15704] VGAM1125 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1125 was detected is described hereinabove with reference to Figs. 2-8.

[15705] VGAM1125 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15706] VGAM1125 gene, herein designated VGAM GENE, encodes



a VGAM1125 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1125 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1125 precursor RNA is designated SEQ ID:29087, and is provided hereinbelow with reference to the sequence listing part.

[15707] VGAM1125 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15708] An enzyme complex designated DICER COMPLEX, dices the VGAM1125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1125 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1125 RNA is designated SEQ ID:29088, and is provided hereinbelow with reference to the sequence listing part.

[15709] VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15710] VGAM1125 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1125 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15711] The complementary binding of VGAM1125 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1125 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[15712] It is appreciated that VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1125 host target genes. The mRNA of each one of this plurality of VGAM1125 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1125 RNA, herein designated VGAM RNA, and which when bound by VGAM1125 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1125 host target proteins.

[15713] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1125 gene, herein designated VGAM GENE, on one or more VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15714] It is yet further appreciated that a function of VGAM1125 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1125 correlate with, and may be deduced from, the identity of the host target genes which VGAM1125 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15715] Nucleotide sequences of the VGAM1125 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1125 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1125 are further described hereinbelow with reference to Table 1.

[15716] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1125 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15717] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1126 (VGAM1126) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15718] VGAM1126 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1126 was detected is described hereinabove with reference to Figs. 2-8.

[15719] VGAM1126 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15720] VGAM1126 gene, herein designated VGAM GENE, encodes a VGAM1126 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1126 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1126 precursor RNA is designated SEQ ID:29108, and is provided hereinbelow with reference to the sequence listing part.

[15721] VGAM1126 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15722] An enzyme complex designated DICER COMPLEX, dices the VGAM1126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1126 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1126 RNA is designated SEQ ID:29109, and is provided hereinbelow with reference to the sequence listing part.

[15723] VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15724] VGAM1126 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host



target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1126 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15725] The complementary binding of VGAM1126 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1126 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15726] It is appreciated that VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1126 host target genes. The mRNA of each one of this plurality of VGAM1126 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1126 RNA, herein designated VGAM RNA, and which when bound by VGAM1126 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1126 host target proteins.

[15727] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1126 gene, herein designated VGAM GENE, on one or more VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15728] It is yet further appreciated that a function of VGAM1126 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1126 correlate with, and may be deduced from, the identity of the host target genes which VGAM1126 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15729] Nucleotide sequences of the VGAM1126 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1126 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1126 are further described hereinbelow with reference to Table 1.

[15730] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1126 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15731] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1127 (VGAM1127) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15732] VGAM1127 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1127 was detected is described hereinabove with reference to Figs. 2-8.

[15733] VGAM1127 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like disease virus. VGAM1127 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15734] VGAM1127 gene, herein designated VGAM GENE, encodes a VGAM1127 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1127 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1127 precursor RNA is designated SEQ ID:29151, and is provided hereinbelow with reference to the sequence listing part.

[15735] VGAM1127 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15736] An enzyme complex designated DICER COMPLEX, dices the VGAM1127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1127 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1127 RNA is designated SEQ ID:29152, and is provided hereinbelow with reference to the sequence listing part.

[15737] VGAM1127 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15738] VGAM1127 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1127 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15739] The complementary binding of VGAM1127 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1127 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15740] It is appreciated that VGAM1127 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1127 host target genes. The mRNA of each one of this plurality of VGAM1127 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1127 RNA, herein designated VGAM RNA, and which when bound by VGAM1127 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1127 host target proteins.

[15741] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1127 gene, herein designated VGAM GENE, on one or more VGAM1127 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15742] It is yet further appreciated that a function of VGAM1127 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of viral infection by Yaba-like disease virus. Specific functions, and accordingly utilities, of VGAM1127 correlate with, and may be deduced from, the identity of the host target genes which VGAM1127 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15743] Nucleotide sequences of the VGAM1127 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1127 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1127 are further described hereinbelow with reference to Table 1.

[15744] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1127 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15745] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1128 (VGAM1128) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15746] VGAM1128 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1128 was detected is described hereinabove with reference to Figs. 2–8.

[15747] VGAM1128 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like disease virus. VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15748] VGAM1128 gene, herein designated VGAM GENE, encodes a VGAM1128 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1128 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1128 precursor RNA is designated SEQ ID:29163, and is provided hereinbelow with reference to the sequence listing part.

[15749] VGAM1128 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15750] An enzyme complex designated DICER COMPLEX, dices the VGAM1128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1128 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1128 RNA is designated SEQ ID:29164, and is provided hereinbelow with reference to the sequence listing part.

[15751] VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15752] VGAM1128 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1128 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15753] The complementary binding of VGAM1128 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1128 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15754] It is appreciated that VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1128 host target genes. The mRNA of each one of this plurality of VGAM1128 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1128 RNA, herein designated VGAM RNA, and which when bound by VGAM1128 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1128 host target proteins.

[15755] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1128 gene, herein designated VGAM GENE, on one or more VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [15756] It is yet further appreciated that a function of VGAM1128 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of viral infection by Yaba-like disease virus. Specific functions, and accordingly utilities, of VGAM1128 correlate with, and may be deduced from, the identity of the host target genes which VGAM1128 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [15757] Nucleotide sequences of the VGAM1128 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1128 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1128 are further described hereinbelow with reference to Table 1.
- [15758] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1128 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15759] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1129 (VGAM1129) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15760] VGAM1129 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1129 was detected is described hereinabove with reference to Figs. 2-8.

[15761] VGAM1129 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15762] VGAM1129 gene, herein designated VGAM GENE, encodes a VGAM1129 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1129 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-



code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1129 precursor RNA is designated SEQ ID:29175, and is provided hereinbelow with reference to the sequence listing part.

[15763] VGAM1129 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15764] An enzyme complex designated DICER COMPLEX, dices the VGAM1129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1129 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1129 RNA is designated SEQ ID:29176, and is provided hereinbelow with reference to the sequence listing part.

[15765] VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15766] VGAM1129 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1129 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15767] The complementary binding of VGAM1129 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1129 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15768] It is appreciated that VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1129 host target genes. The mRNA of

each one of this plurality of VGAM1129 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1129 RNA, herein designated VGAM RNA, and which when bound by VGAM1129 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1129 host target proteins.

[15769] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1129 gene, herein designated VGAM GENE, on one or more VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[15770] It is yet further appreciated that a function of VGAM1129 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1129 correlate with, and may be deduced from, the identity of the host target genes which VGAM1129 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15771] Nucleotide sequences of the VGAM1129 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1129 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1129 are further described hereinbelow with reference to Table 1.

[15772] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1129 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[15773] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1130 (VGAM1130) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15774] VGAM1130 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1130 was detected is described hereinabove with reference to Figs. 2–8.

[15775] VGAM1130 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15776] VGAM1130 gene, herein designated VGAM GENE, encodes a VGAM1130 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1130 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1130 precursor RNA is designated SEQ ID:29285, and is provided hereinbelow with reference to the sequence listing part.

[15777] VGAM1130 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15778] An enzyme complex designated DICER COMPLEX, dices the VGAM1130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1130 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1130 RNA is designated SEQ ID:29286,

and is provided hereinbelow with reference to the sequence listing part.

[15779] VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15780] VGAM1130 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1130 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1130 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15781] The complementary binding of VGAM1130 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1130 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15782] It is appreciated that VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1130 host target genes. The mRNA of each one of this plurality of VGAM1130 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1130 RNA, herein designated VGAM RNA, and which when bound by VGAM1130 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1130 host target proteins.

[15783] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1130 gene, herein designated VGAM GENE, on one or more VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15784] It is yet further appreciated that a function of VGAM1130 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1130 correlate with, and may be deduced from, the identity of the host target genes which VGAM1130 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15785] Nucleotide sequences of the VGAM1130 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1130 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1130 are further described hereinbelow with reference to Table 1.

[15786] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1130 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15787] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1131 (VGAM1131) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15788] VGAM1131 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1131 was detected is described hereinabove with reference to Figs. 2–8.

[15789] VGAM1131 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15790] VGAM1131 gene, herein designated VGAM GENE, encodes a VGAM1131 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1131 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1131 precu-

sor RNA is designated SEQ ID:29305, and is provided hereinbelow with reference to the sequence listing part.

[15791] VGAM1131 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15792] An enzyme complex designated DICER COMPLEX, dices the VGAM1131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1131 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1131 RNA is designated SEQ ID:29306, and is provided hereinbelow with reference to the se-

quence listing part.

[15793] VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15794] VGAM1131 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1131 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15795] The complementary binding of VGAM1131 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1131 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15796] It is appreciated that VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1131 host target genes. The mRNA of each one of this plurality of VGAM1131 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1131 RNA, herein designated VGAM RNA, and which when bound by VGAM1131 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1131 host target proteins.

[15797] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1131 gene, herein designated VGAM GENE, on one or more VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15798] It is yet further appreciated that a function of VGAM1131



is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1131 correlate with, and may be deduced from, the identity of the host target genes which VGAM1131 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15799] Nucleotide sequences of the VGAM1131 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1131 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1131 are further described hereinbelow with reference to Table 1.

[15800] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1131 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15801] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1132 (VGAM1132) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15802] VGAM1132 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1132 was detected is described hereinabove with reference to Figs. 2–8.

[15803] VGAM1132 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15804] VGAM1132 gene, herein designated VGAM GENE, encodes a VGAM1132 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1132 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1132 precursor RNA is designated SEQ ID:29310, and is provided

hereinbelow with reference to the sequence listing part.

[15805] VGAM1132 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15806] An enzyme complex designated DICER COMPLEX, dices the VGAM1132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1132 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1132 RNA is designated SEQ ID:29311, and is provided hereinbelow with reference to the sequence listing part.

[15807] VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15808] VGAM1132 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1132 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15809] The complementary binding of VGAM1132 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1132 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15810] It is appreciated that VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1132 host target genes. The mRNA of each one of this plurality of VGAM1132 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1132 RNA, herein designated VGAM RNA, and which when bound by VGAM1132 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1132 host target proteins.

[15811] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1132 gene, herein designated VGAM GENE, on one or more VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15812] It is yet further appreciated that a function of VGAM1132 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1132 correlate with, and may be deduced from, the identity of the host target genes which VGAM1132 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15813] Nucleotide sequences of the VGAM1132 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1132 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1132 are further described hereinbelow with reference to Table 1.

[15814] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1132 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15815] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1133 (VGAM1133) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15816] VGAM1133 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1133 was detected is described hereinabove with reference to Figs. 2–8.

[15817] VGAM1133 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1133 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15818] VGAM1133 gene, herein designated VGAM GENE, encodes a VGAM1133 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1133 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1133 precursor RNA is designated SEQ ID:29322, and is provided hereinbelow with reference to the sequence listing part.



[15819] VGAM1133 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15820] An enzyme complex designated DICER COMPLEX, dices the VGAM1133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1133 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1133 RNA is designated SEQ ID:29323, and is provided hereinbelow with reference to the sequence listing part.

[15821] VGAM1133 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15822] VGAM1133 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1133 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15823] The complementary binding of VGAM1133 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1133 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15824] It is appreciated that VGAM1133 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1133 host target genes. The mRNA of each one of this plurality of VGAM1133 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1133 RNA, herein designated VGAM

RNA, and which when bound by VGAM1133 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1133 host target proteins.

[15825] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1133 gene, herein designated VGAM GENE, on one or more VGAM1133 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15826] It is yet further appreciated that a function of VGAM1133 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1133 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1133 correlate with, and may be deduced from, the identity of the host target genes which VGAM1133 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15827] Nucleotide sequences of the VGAM1133 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1133 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1133 are further described hereinbelow with reference to Table 1.

[15828] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1133 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15829] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1134 (VGAM1134) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15830] VGAM1134 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1134 was detected is described hereinabove with reference to Figs. 2-8.

[15831] VGAM1134 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15832] VGAM1134 gene, herein designated VGAM GENE, encodes a VGAM1134 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1134 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1134 precursor RNA is designated SEQ ID:29336, and is provided hereinbelow with reference to the sequence listing part.

[15833] VGAM1134 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15834] An enzyme complex designated DICER COMPLEX, dices the VGAM1134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1134 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1134 RNA is designated SEQ ID:29337, and is provided hereinbelow with reference to the sequence listing part.

[15835] VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15836] VGAM1134 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1134 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1134 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1134 host



target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15837] The complementary binding of VGAM1134 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1134 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15838] It is appreciated that VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1134 host target genes. The mRNA of each one of this plurality of VGAM1134 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1134 RNA, herein designated VGAM RNA, and which when bound by VGAM1134 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1134 host target proteins.

[15839] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1134 gene, herein designated VGAM GENE, on one or more VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15840] It is yet further appreciated that a function of VGAM1134 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1134 include diagnosis, prevention and

treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1134 correlate with, and may be deduced from, the identity of the host target genes which VGAM1134 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15841] Nucleotide sequences of the VGAM1134 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1134 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1134 are further described hereinbelow with reference to Table 1.

[15842] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1134 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15843] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1135 (VGAM1135) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15844] VGAM1135 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1135 was detected is described hereinabove with reference to Figs. 2–8.

[15845] VGAM1135 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1135 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15846] VGAM1135 gene, herein designated VGAM GENE, encodes a VGAM1135 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1135 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1135 precursor RNA is designated SEQ ID:29357, and is provided hereinbelow with reference to the sequence listing part.

[15847] VGAM1135 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1135 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15848] An enzyme complex designated DICER COMPLEX, dices the VGAM1135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1135 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1135 RNA is designated SEQ ID:29358, and is provided hereinbelow with reference to the sequence listing part.

[15849] VGAM1135 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1135 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15850] VGAM1135 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1135 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15851] The complementary binding of VGAM1135 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1135 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15852] It is appreciated that VGAM1135 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1135 host target genes. The mRNA of each one of this plurality of VGAM1135 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1135 RNA, herein designated VGAM RNA, and which when bound by VGAM1135 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1135 host target proteins.

[15853] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1135 gene, herein designated VGAM GENE, on one or more VGAM1135 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15854] It is yet further appreciated that a function of VGAM1135 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Spe-



cific functions, and accordingly utilities, of VGAM1135 correlate with, and may be deduced from, the identity of the host target genes which VGAM1135 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15855] Nucleotide sequences of the VGAM1135 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1135 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1135 are further described hereinbelow with reference to Table 1.

[15856] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1135 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15857] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1136 (VGAM1136) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[15858] VGAM1136 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1136 was detected is described hereinabove with reference to Figs. 2–8.

[15859] VGAM1136 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15860] VGAM1136 gene, herein designated VGAM GENE, encodes a VGAM1136 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1136 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1136 precursor RNA is designated SEQ ID:29367, and is provided hereinbelow with reference to the sequence listing part.

[15861] VGAM1136 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1136 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15862] An enzyme complex designated DICER COMPLEX, dices the VGAM1136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1136 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1136 RNA is designated SEQ ID:29368, and is provided hereinbelow with reference to the sequence listing part.

[15863] VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1136 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15864] VGAM1136 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1136 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1136 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15865] The complementary binding of VGAM1136 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1136 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15866] It is appreciated that VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1136 host target genes. The mRNA of each one of this plurality of VGAM1136 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1136 RNA, herein designated VGAM RNA, and which when bound by VGAM1136 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1136 host target proteins.

[15867] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1136 gene, herein designated VGAM GENE, on one or more VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15868] It is yet further appreciated that a function of VGAM1136 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1136 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1136

correlate with, and may be deduced from, the identity of the host target genes which VGAM1136 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15869] Nucleotide sequences of the VGAM1136 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1136 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1136 are further described hereinbelow with reference to Table 1.

[15870] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1136 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15871] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1137 (VGAM1137) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[15872] VGAM1137 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1137 was detected is described hereinabove with reference to Figs. 2–8.

[15873] VGAM1137 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15874] VGAM1137 gene, herein designated VGAM GENE, encodes a VGAM1137 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1137 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1137 precursor RNA is designated SEQ ID:29374, and is provided hereinbelow with reference to the sequence listing part.

[15875] VGAM1137 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.



As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15876] An enzyme complex designated DICER COMPLEX, dices the VGAM1137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1137 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1137 RNA is designated SEQ ID:29375, and is provided hereinbelow with reference to the sequence listing part.

[15877] VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15878] VGAM1137 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1137 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1137 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15879] The complementary binding of VGAM1137 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1137 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15880] It is appreciated that VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1137 host target genes. The mRNA of each one of this plurality of VGAM1137 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1137 RNA, herein designated VGAM RNA, and which when bound by VGAM1137 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1137 host target proteins.

[15881] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1137 gene, herein designated VGAM GENE, on one or more VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15882] It is yet further appreciated that a function of VGAM1137 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1137 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1137 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1137 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15883] Nucleotide sequences of the VGAM1137 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1137 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1137 are further described hereinbelow with reference to Table 1.

[15884] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1137 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15885] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1138 (VGAM1138) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15886] VGAM1138 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1138 was detected is described hereinabove with reference to Figs. 2-8.

[15887] VGAM1138 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15888] VGAM1138 gene, herein designated VGAM GENE, encodes a VGAM1138 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1138 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1138 precursor RNA is designated SEQ ID:29387, and is provided hereinbelow with reference to the sequence listing part.

[15889] VGAM1138 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15890] An enzyme complex designated DICER COMPLEX, dices the VGAM1138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1138 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1138 RNA is designated SEQ ID:29388, and is provided hereinbelow with reference to the sequence listing part.

[15891] VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15892] VGAM1138 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1138 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-



cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15893] The complementary binding of VGAM1138 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1138 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15894] It is appreciated that VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1138 host target genes. The mRNA of each one of this plurality of VGAM1138 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1138 RNA, herein designated VGAM RNA, and which when bound by VGAM1138 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1138 host target proteins.

[15895] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1138 gene, herein designated VGAM GENE, on one or more VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15896] It is yet further appreciated that a function of VGAM1138 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1138 correlate with, and may be deduced from, the identity of the host target genes which VGAM1138 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[15897] Nucleotide sequences of the VGAM1138 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1138 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1138 are further described hereinbelow with reference to Table 1.

[15898] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1138 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15899] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1139 (VGAM1139) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15900] VGAM1139 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1139 was detected is described hereinabove with reference to Figs. 2–8.

[15901] VGAM1139 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15902] VGAM1139 gene, herein designated VGAM GENE, encodes a VGAM1139 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1139 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1139 precursor RNA is designated SEQ ID:29395, and is provided hereinbelow with reference to the sequence listing part.

[15903] VGAM1139 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15904] An enzyme complex designated DICER COMPLEX, dices the VGAM1139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1139 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1139 RNA is designated SEQ ID:29396, and is provided hereinbelow with reference to the sequence listing part.

[15905] VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15906] VGAM1139 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1139 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1139 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[15907] The complementary binding of VGAM1139 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1139 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15908] It is appreciated that VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1139 host target genes. The mRNA of each one of this plurality of VGAM1139 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1139 RNA, herein designated VGAM RNA, and which when bound by VGAM1139 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1139 host target proteins.

[15909] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1139 gene, herein designated VGAM GENE, on one or more VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15910] It is yet further appreciated that a function of VGAM1139 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1139 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1139 correlate with, and may be deduced from, the identity of the host target genes which VGAM1139 binds and inhibits, and the function of these host target genes, as



elaborated hereinbelow.

[15911] Nucleotide sequences of the VGAM1139 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1139 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1139 are further described hereinbelow with reference to Table 1.

[15912] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1139 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15913] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1140 (VGAM1140) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15914] VGAM1140 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1140 was detected is described hereinabove with reference to Figs. 2–8.

[15915] VGAM1140 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15916] VGAM1140 gene, herein designated VGAM GENE, encodes a VGAM1140 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1140 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1140 precursor RNA is designated SEQ ID:29403, and is provided hereinbelow with reference to the sequence listing part.

[15917] VGAM1140 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15918] An enzyme complex designated DICER COMPLEX, dices the VGAM1140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1140 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1140 RNA is designated SEQ ID:29404, and is provided hereinbelow with reference to the sequence listing part.

[15919] VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[15920] VGAM1140 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1140 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1140 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15921] The complementary binding of VGAM1140 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1140 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15922] It is appreciated that VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1140 host target genes. The mRNA of each one of this plurality of VGAM1140 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1140 RNA, herein designated VGAM RNA, and which when bound by VGAM1140 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1140 host target proteins.

[15923] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1140 gene, herein designated VGAM GENE, on one

or more VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15924] It is yet further appreciated that a function of VGAM1140 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1140 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1140 correlate with, and may be deduced from, the identity of the host target genes which VGAM1140 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15925] Nucleotide sequences of the VGAM1140 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1140 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1140 are further described hereinbelow with reference to Table 1.

[15926] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1140 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15927] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1141 (VGAM1141) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15928] VGAM1141 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1141 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[15929] VGAM1141 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM1141 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15930] VGAM1141 gene, herein designated VGAM GENE, encodes a VGAM1141 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1141 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1141 precursor RNA is designated SEQ ID:29412, and is provided hereinbelow with reference to the sequence listing part.

[15931] VGAM1141 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15932] An enzyme complex designated DICER COMPLEX, dices the VGAM1141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1141 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1141 RNA is designated SEQ ID:29413, and is provided hereinbelow with reference to the sequence listing part.

[15933] VGAM1141 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15934] VGAM1141 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1141 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1141 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15935] The complementary binding of VGAM1141 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1141 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15936] It is appreciated that VGAM1141 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1141 host target genes. The mRNA of each one of this plurality of VGAM1141 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1141 RNA, herein designated VGAM RNA, and which when bound by VGAM1141 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1141 host target proteins.

[15937] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1141 gene, herein designated VGAM GENE, on one or more VGAM1141 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15938] It is yet further appreciated that a function of VGAM1141 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1141 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM1141 correlate with, and may be deduced from, the identity of the host target genes which VGAM1141 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15939] Nucleotide sequences of the VGAM1141 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1141 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1141 are further described hereinbelow with reference to Table 1.

[15940] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1141 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15941] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1142 (VGAM1142) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15942] VGAM1142 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1142 was detected is described hereinabove with reference to Figs. 2-8.

[15943] VGAM1142 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15944] VGAM1142 gene, herein designated VGAM GENE, encodes a VGAM1142 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1142 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1142 precursor RNA is designated SEQ ID:29425, and is provided hereinbelow with reference to the sequence listing part.

[15945] VGAM1142 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[15946] An enzyme complex designated DICER COMPLEX, dices the VGAM1142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1142 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1142 RNA is designated SEQ ID:29426, and is provided hereinbelow with reference to the sequence listing part.

[15947] VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15948] VGAM1142 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1142 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15949] The complementary binding of VGAM1142 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1142 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15950] It is appreciated that VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1142 host target genes. The mRNA of each one of this plurality of VGAM1142 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1142 RNA, herein designated VGAM RNA, and which when bound by VGAM1142 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1142 host target proteins.

[15951] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1142 gene, herein designated VGAM GENE, on one or more VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15952] It is yet further appreciated that a function of VGAM1142 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1142 correlate with, and may be deduced from, the identity of the host target genes which VGAM1142 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15953] Nucleotide sequences of the VGAM1142 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1142 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1142 are further described hereinbelow with reference to Table 1.

[15954] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1142 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15955] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1143 (VGAM1143) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15956] VGAM1143 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1143 was detected is described hereinabove with reference to Figs. 2-8.

[15957] VGAM1143 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Rat cytomegalovirus. VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15958] VGAM1143 gene, herein designated VGAM GENE, encodes a VGAM1143 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1143 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1143 precursor RNA is designated SEQ ID:29435, and is provided hereinbelow with reference to the sequence listing part.

[15959] VGAM1143 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15960] An enzyme complex designated DICER COMPLEX, dices the VGAM1143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1143 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1143 RNA is designated SEQ ID:29436, and is provided hereinbelow with reference to the sequence listing part.

[15961] VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15962] VGAM1143 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1143 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1143 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15963] The complementary binding of VGAM1143 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1143 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1143 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15964] It is appreciated that VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1143 host target genes. The mRNA of each one of this plurality of VGAM1143 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1143 RNA, herein designated VGAM RNA, and which when bound by VGAM1143 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1143 host target proteins.

[15965] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1143 gene, herein designated VGAM GENE, on one or more VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15966] It is yet further appreciated that a function of VGAM1143 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1143 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1143 correlate with, and may be deduced from, the identity of the host target genes which VGAM1143 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15967] Nucleotide sequences of the VGAM1143 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1143 RNA, herein designated VGAM RNA, and



a schematic representation of the secondary folding of VGAM1143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1143 are further described hereinbelow with reference to Table 1.

[15968] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1143 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15969] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1144 (VGAM1144) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15970] VGAM1144 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1144 was detected is described hereinabove with reference to Figs. 2-8.

[15971] VGAM1144 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus

type 45. VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15972] VGAM1144 gene, herein designated VGAM GENE, encodes a VGAM1144 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1144 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1144 precursor RNA is designated SEQ ID:29771, and is provided hereinbelow with reference to the sequence listing part.

[15973] VGAM1144 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15974] An enzyme complex designated DICER COMPLEX, dices

the VGAM1144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1144 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1144 RNA is designated SEQ ID:29772, and is provided hereinbelow with reference to the sequence listing part.

[15975] VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15976] VGAM1144 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1144 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1144 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1144 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15977] The complementary binding of VGAM1144 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1144 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15978] It is appreciated that VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1144 host target genes. The mRNA of each one of this plurality of VGAM1144 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1144 RNA, herein designated VGAM RNA, and which when bound by VGAM1144 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1144 host target proteins.

[15979] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1144 gene, herein designated VGAM GENE, on one or more VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15980] It is yet further appreciated that a function of VGAM1144 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 45. Specific functions, and accordingly utilities, of VGAM1144 correlate with, and may be deduced from, the identity of the host target genes which VGAM1144 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15981] Nucleotide sequences of the VGAM1144 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1144 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1144 are further described hereinbelow with reference to Table 1.

[15982] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1144 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15983] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1145 (VGAM1145) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15984] VGAM1145 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1145 was detected is described hereinabove with reference to Figs. 2-8.

[15985] VGAM1145 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 45. VGAM1145 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15986] VGAM1145 gene, herein designated VGAM GENE, encodes a VGAM1145 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1145 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1145 precursor RNA is designated SEQ ID:29785, and is provided hereinbelow with reference to the sequence listing part.

[15987] VGAM1145 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15988] An enzyme complex designated DICER COMPLEX, dices the VGAM1145 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM1145 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1145 RNA is designated SEQ ID:29786, and is provided hereinbelow with reference to the sequence listing part.

[15989] VGAM1145 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[15990] VGAM1145 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1145 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1145 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[15991] The complementary binding of VGAM1145 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1145

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1145 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15992] It is appreciated that VGAM1145 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1145 host target genes. The mRNA of each one of this plurality of VGAM1145 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1145 RNA, herein designated VGAM RNA, and which when bound by VGAM1145 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1145 host target proteins.

[15993] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1145 gene, herein designated VGAM GENE, on one or more VGAM1145 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[15994] It is yet further appreciated that a function of VGAM1145 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1145 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 45. Specific functions, and accordingly utilities, of VGAM1145 correlate with, and may be deduced from, the identity of the host target genes which VGAM1145 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15995] Nucleotide sequences of the VGAM1145 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1145 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1145 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1145 are further described hereinbelow with reference to Table 1.

[15996] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1145 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15997] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1146 (VGAM1146) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15998] VGAM1146 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1146 was detected is described hereinabove with reference to Figs. 2-8.

[15999] VGAM1146 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 45. VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[16000] VGAM1146 gene, herein designated VGAM GENE, encodes a VGAM1146 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1146 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1146 precursor RNA is designated SEQ ID:29790, and is provided hereinbelow with reference to the sequence listing part.

[16001] VGAM1146 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16002] An enzyme complex designated DICER COMPLEX, dices the VGAM1146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1146 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1146 RNA is designated SEQ ID:29791, and is provided hereinbelow with reference to the sequence listing part.

[16003] VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16004] VGAM1146 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1146 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16005] The complementary binding of VGAM1146 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1146 host target RNA, herein designated VGAM HOST TARGET



RNA, into VGAM1146 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16006] It is appreciated that VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1146 host target genes. The mRNA of each one of this plurality of VGAM1146 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1146 RNA, herein designated VGAM RNA, and which when bound by VGAM1146 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1146 host target proteins.

[16007] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1146 gene, herein designated VGAM GENE, on one or more VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16008] It is yet further appreciated that a function of VGAM1146 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 45. Specific functions, and accordingly utilities, of VGAM1146 correlate with, and may be deduced from, the identity of the host target genes which VGAM1146 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16009] Nucleotide sequences of the VGAM1146 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1146 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1146 are further

described hereinbelow with reference to Table 1.

[16010] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1146 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16011] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1147 (VGAM1147) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16012] VGAM1147 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1147 was detected is described hereinabove with reference to Figs. 2-8.

[16013] VGAM1147 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 45. VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16014] VGAM1147 gene, herein designated VGAM GENE, encodes a VGAM1147 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1147 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1147 precursor RNA is designated SEQ ID:29823, and is provided hereinbelow with reference to the sequence listing part.

[16015] VGAM1147 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16016] An enzyme complex designated DICER COMPLEX, dices the VGAM1147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1147 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1147 RNA is designated SEQ ID:29824, and is provided hereinbelow with reference to the sequence listing part.

[16017] VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16018] VGAM1147 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1147 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1147 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16019] The complementary binding of VGAM1147 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1147 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16020] It is appreciated that VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1147 host target genes. The mRNA of each one of this plurality of VGAM1147 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1147 RNA, herein designated VGAM RNA, and which when bound by VGAM1147 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1147 host target proteins.

[16021] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1147 gene, herein designated VGAM GENE, on one or more VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16022] It is yet further appreciated that a function of VGAM1147 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1147 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 45. Specific functions, and accordingly utilities, of VGAM1147 correlate with, and may be deduced from, the identity of the host target genes which VGAM1147 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16023] Nucleotide sequences of the VGAM1147 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1147 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1147 are further described hereinbelow with reference to Table 1.



[16024] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1147 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16025] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1148 (VGAM1148) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16026] VGAM1148 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1148 was detected is described hereinabove with reference to Figs. 2-8.

[16027] VGAM1148 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16028] VGAM1148 gene, herein designated VGAM GENE, encodes

a VGAM1148 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1148 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1148 precursor RNA is designated SEQ ID:29834, and is provided hereinbelow with reference to the sequence listing part.

[16029] VGAM1148 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16030] An enzyme complex designated DICER COMPLEX, dices the VGAM1148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1148 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1148 RNA is designated SEQ ID:29835, and is provided hereinbelow with reference to the sequence listing part.

[16031] VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16032] VGAM1148 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1148 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16033] The complementary binding of VGAM1148 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1148 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[16034] It is appreciated that VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1148 host target genes. The mRNA of each one of this plurality of VGAM1148 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1148 RNA, herein designated VGAM RNA, and which when bound by VGAM1148 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1148 host target proteins.

[16035] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1148 gene, herein designated VGAM GENE, on one or more VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16036] It is yet further appreciated that a function of VGAM1148 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM1148 correlate with, and may be deduced from, the identity of the host target genes which VGAM1148 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16037] Nucleotide sequences of the VGAM1148 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1148 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1148 are further described hereinbelow with reference to Table 1.

[16038] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1148 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16039] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1149 (VGAM1149) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16040] VGAM1149 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1149 was detected is described hereinabove with reference to Figs. 2-8.

[16041] VGAM1149 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16042] VGAM1149 gene, herein designated VGAM GENE, encodes a VGAM1149 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1149 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1149 precursor RNA is designated SEQ ID:29844, and is provided hereinbelow with reference to the sequence listing part.

[16043] VGAM1149 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16044] An enzyme complex designated DICER COMPLEX, dices the VGAM1149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1149 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1149 RNA is designated SEQ ID:29845, and is provided hereinbelow with reference to the sequence listing part.

[16045] VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16046] VGAM1149 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1149 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1149 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16047] The complementary binding of VGAM1149 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1149 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16048] It is appreciated that VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1149 host target genes. The mRNA of each one of this plurality of VGAM1149 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1149 RNA, herein designated VGAM RNA, and which when bound by VGAM1149 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1149 host target proteins.

[16049] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1149 gene, herein designated VGAM GENE, on one or more VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16050] It is yet further appreciated that a function of VGAM1149 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1149 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM1149 correlate with, and may be deduced from, the identity of the host target genes which VGAM1149 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16051] Nucleotide sequences of the VGAM1149 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1149 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1149 are further described hereinbelow with reference to Table 1.

[16052] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1149 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16053] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1150 (VGAM1150) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16054] VGAM1150 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1150 was detected is described hereinabove with reference to Figs. 2-8.

[16055] VGAM1150 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM1150 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16056] VGAM1150 gene, herein designated VGAM GENE, encodes a VGAM1150 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1150 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1150 precursor RNA is designated SEQ ID:29858, and is provided hereinbelow with reference to the sequence listing part.

[16057] VGAM1150 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16058] An enzyme complex designated DICER COMPLEX, dices the VGAM1150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1150 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1150 RNA is designated SEQ ID:29859, and is provided hereinbelow with reference to the sequence listing part.

[16059] VGAM1150 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16060] VGAM1150 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1150 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1150 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16061] The complementary binding of VGAM1150 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1150 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16062] It is appreciated that VGAM1150 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1150 host target genes. The mRNA of each one of this plurality of VGAM1150 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1150 RNA, herein designated VGAM RNA, and which when bound by VGAM1150 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1150 host target proteins.

[16063] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1150 gene, herein designated VGAM GENE, on one or more VGAM1150 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16064] It is yet further appreciated that a function of VGAM1150 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1150 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM1150 correlate with, and may be deduced from, the identity of the host target genes which VGAM1150 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16065] Nucleotide sequences of the VGAM1150 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1150 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1150 are further described hereinbelow with reference to Table 1.

[16066] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1150 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16067] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1151 (VGAM1151) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16068] VGAM1151 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1151 was detected is described hereinabove with reference to Figs. 2–8.

[16069] VGAM1151 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 56. VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16070] VGAM1151 gene, herein designated VGAM GENE, encodes a VGAM1151 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1151 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1151 precursor RNA is designated SEQ ID:29864, and is provided hereinbelow with reference to the sequence listing part.

[16071] VGAM1151 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16072] An enzyme complex designated DICER COMPLEX, dices the VGAM1151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1151 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1151 RNA is designated SEQ ID:29865, and is provided hereinbelow with reference to the sequence listing part.

[16073] VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16074] VGAM1151 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1151 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16075] The complementary binding of VGAM1151 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1151 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16076] It is appreciated that VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1151 host target genes. The mRNA of each one of this plurality of VGAM1151 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1151 RNA, herein designated VGAM RNA, and which when bound by VGAM1151 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1151 host target proteins.

[16077] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1151 gene, herein designated VGAM GENE, on one or more VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[16078] It is yet further appreciated that a function of VGAM1151 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 56. Specific functions, and accordingly utilities, of VGAM1151 correlate with, and may be deduced from, the identity of the host target genes which VGAM1151 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16079] Nucleotide sequences of the VGAM1151 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1151 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1151 are further described hereinbelow with reference to Table 1.

[16080] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM1151 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16081] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1152 (VGAM1152) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16082] VGAM1152 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1152 was detected is described hereinabove with reference to Figs. 2-8.

[16083] VGAM1152 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 56. VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16084] VGAM1152 gene, herein designated VGAM GENE, encodes a VGAM1152 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1152 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1152 precursor RNA is designated SEQ ID:29874, and is provided hereinbelow with reference to the sequence listing part.

[16085] VGAM1152 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16086] An enzyme complex designated DICER COMPLEX, dices the VGAM1152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1152 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM1152 RNA is designated SEQ ID:29875, and is provided hereinbelow with reference to the sequence listing part.

[16087] VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16088] VGAM1152 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1152 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16089] The complementary binding of VGAM1152 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1152 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16090] It is appreciated that VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1152 host target genes. The mRNA of

each one of this plurality of VGAM1152 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1152 RNA, herein designated VGAM RNA, and which when bound by VGAM1152 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1152 host target proteins.

[16091] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1152 gene, herein designated VGAM GENE, on one or more VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[16092] It is yet further appreciated that a function of VGAM1152 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 56. Specific functions, and accordingly utilities, of VGAM1152 correlate with, and may be deduced from, the identity of the host target genes which VGAM1152 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16093] Nucleotide sequences of the VGAM1152 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1152 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1152 are further described hereinbelow with reference to Table 1.

[16094] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1152 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[16095] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1153 (VGAM1153) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16096] VGAM1153 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1153 was detected is described hereinabove with reference to Figs. 2–8.

[16097] VGAM1153 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 56. VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16098] VGAM1153 gene, herein designated VGAM GENE, encodes a VGAM1153 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1153 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1153 precursor RNA is designated SEQ ID:29897, and is provided hereinbelow with reference to the sequence listing part.

[16099] VGAM1153 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16100] An enzyme complex designated DICER COMPLEX, dices the VGAM1153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1153 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1153 RNA is designated SEQ ID:29898,



and is provided hereinbelow with reference to the sequence listing part.

[16101] VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16102] VGAM1153 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1153 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1153 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16103] The complementary binding of VGAM1153 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1153 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16104] It is appreciated that VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1153 host target genes. The mRNA of each one of this plurality of VGAM1153 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1153 RNA, herein designated VGAM RNA, and which when bound by VGAM1153 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1153 host target proteins.

[16105] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1153 gene, herein designated VGAM GENE, on one or more VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16106] It is yet further appreciated that a function of VGAM1153 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1153 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 56. Specific functions, and accordingly utilities, of VGAM1153 correlate with, and may be deduced from, the identity of the host target genes which VGAM1153 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16107] Nucleotide sequences of the VGAM1153 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1153 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1153 are further described hereinbelow with reference to Table 1.

[16108] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1153 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16109] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1154 (VGAM1154) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16110] VGAM1154 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1154 was detected is described hereinabove with reference to Figs. 2–8.

[16111] VGAM1154 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 56. VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16112] VGAM1154 gene, herein designated VGAM GENE, encodes a VGAM1154 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1154 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1154 precu-

sor RNA is designated SEQ ID:29917, and is provided hereinbelow with reference to the sequence listing part.

[16113] VGAM1154 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16114] An enzyme complex designated DICER COMPLEX, dices the VGAM1154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1154 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1154 RNA is designated SEQ ID:29918, and is provided hereinbelow with reference to the se-

quence listing part.

[16115] VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16116] VGAM1154 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1154 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1154 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16117] The complementary binding of VGAM1154 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1154 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16118] It is appreciated that VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1154 host target genes. The mRNA of each one of this plurality of VGAM1154 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1154 RNA, herein designated VGAM RNA, and which when bound by VGAM1154 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1154 host target proteins.

[16119] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1154 gene, herein designated VGAM GENE, on one or more VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16120] It is yet further appreciated that a function of VGAM1154

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1154 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 56. Specific functions, and accordingly utilities, of VGAM1154 correlate with, and may be deduced from, the identity of the host target genes which VGAM1154 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16121] Nucleotide sequences of the VGAM1154 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1154 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1154 are further described hereinbelow with reference to Table 1.

[16122] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1154 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16123] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1155 (VGAM1155) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16124] VGAM1155 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1155 was detected is described hereinabove with reference to Figs. 2–8.

[16125] VGAM1155 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 18. VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16126] VGAM1155 gene, herein designated VGAM GENE, encodes a VGAM1155 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1155 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1155 precursor RNA is designated SEQ ID:29924, and is provided

hereinbelow with reference to the sequence listing part.

[16127] VGAM1155 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16128] An enzyme complex designated DICER COMPLEX, dices the VGAM1155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1155 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1155 RNA is designated SEQ ID:29925, and is provided hereinbelow with reference to the sequence listing part.

[16129] VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16130] VGAM1155 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1155 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16131] The complementary binding of VGAM1155 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1155 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16132] It is appreciated that VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1155 host target genes. The mRNA of each one of this plurality of VGAM1155 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1155 RNA, herein designated VGAM RNA, and which when bound by VGAM1155 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1155 host target proteins.

[16133] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1155 gene, herein designated VGAM GENE, on one or more VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16134] It is yet further appreciated that a function of VGAM1155 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 18. Specific functions, and accordingly utilities, of VGAM1155 correlate with, and may be deduced from, the identity of the host target genes which VGAM1155 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16135] Nucleotide sequences of the VGAM1155 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1155 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1155 are further described hereinbelow with reference to Table 1.

[16136] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1155 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16137] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 1156 (VGAM1156) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16138] VGAM1156 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1156 was detected is described hereinabove with reference to Figs. 2–8.

[16139] VGAM1156 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1156 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16140] VGAM1156 gene, herein designated VGAM GENE, encodes a VGAM1156 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1156 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1156 precursor RNA is designated SEQ ID:29944, and is provided hereinbelow with reference to the sequence listing part.

[16141] VGAM1156 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16142] An enzyme complex designated DICER COMPLEX, dices the VGAM1156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1156 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1156 RNA is designated SEQ ID:29945, and is provided hereinbelow with reference to the sequence listing part.

[16143] VGAM1156 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16144] VGAM1156 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1156 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16145] The complementary binding of VGAM1156 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1156 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16146] It is appreciated that VGAM1156 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1156 host target genes. The mRNA of each one of this plurality of VGAM1156 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1156 RNA, herein designated VGAM

RNA, and which when bound by VGAM1156 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1156 host target proteins.

[16147] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1156 gene, herein designated VGAM GENE, on one or more VGAM1156 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16148] It is yet further appreciated that a function of VGAM1156 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1156 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1156 correlate with, and may be deduced from, the identity of the host target genes which VGAM1156 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16149] Nucleotide sequences of the VGAM1156 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1156 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1156 are further described hereinbelow with reference to Table 1.

[16150] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1156 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16151] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1157 (VGAM1157) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16152] VGAM1157 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1157 was detected is described hereinabove with reference to Figs. 2–8.

[16153] VGAM1157 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16154] VGAM1157 gene, herein designated VGAM GENE, encodes a VGAM1157 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1157 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1157 precursor RNA is designated SEQ ID:29950, and is provided hereinbelow with reference to the sequence listing part.

[16155] VGAM1157 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16156] An enzyme complex designated DICER COMPLEX, dices the VGAM1157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1157 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1157 RNA is designated SEQ ID:29951, and is provided hereinbelow with reference to the sequence listing part.

[16157] VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16158] VGAM1157 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1157 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1157 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1157 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16159] The complementary binding of VGAM1157 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1157 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16160] It is appreciated that VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1157 host target genes. The mRNA of each one of this plurality of VGAM1157 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1157 RNA, herein designated VGAM RNA, and which when bound by VGAM1157 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1157 host target proteins.

[16161] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1157 gene, herein designated VGAM GENE, on one or more VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16162] It is yet further appreciated that a function of VGAM1157 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1157 include diagnosis, prevention and

treatment of viral infection by Meleagrid herpesvirus 1.

Specific functions, and accordingly utilities, of VGAM1157 correlate with, and may be deduced from, the identity of the host target genes which VGAM1157 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16163] Nucleotide sequences of the VGAM1157 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1157 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1157 are further described hereinbelow with reference to Table 1.

[16164] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1157 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16165] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1158 (VGAM1158) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16166] VGAM1158 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1158 was detected is described hereinabove with reference to Figs. 2–8.

[16167] VGAM1158 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 18. VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16168] VGAM1158 gene, herein designated VGAM GENE, encodes a VGAM1158 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1158 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1158 precursor RNA is designated SEQ ID:29954, and is provided hereinbelow with reference to the sequence listing part.

[16169] VGAM1158 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1158 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16170] An enzyme complex designated DICER COMPLEX, dices the VGAM1158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1158 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1158 RNA is designated SEQ ID:29955, and is provided hereinbelow with reference to the sequence listing part.

[16171] VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1158 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16172] VGAM1158 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1158 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16173] The complementary binding of VGAM1158 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1158 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16174] It is appreciated that VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1158 host target genes. The mRNA of each one of this plurality of VGAM1158 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1158 RNA, herein designated VGAM RNA, and which when bound by VGAM1158 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM1158 host target proteins.

[16175] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1158 gene, herein designated VGAM GENE, on one or more VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16176] It is yet further appreciated that a function of VGAM1158 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type

18. Specific functions, and accordingly utilities, of VGAM1158 correlate with, and may be deduced from, the identity of the host target genes which VGAM1158 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16177] Nucleotide sequences of the VGAM1158 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1158 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1158 are further described hereinbelow with reference to Table 1.

[16178] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1158 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16179] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1159 (VGAM1159) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[16180] VGAM1159 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1159 was detected is described hereinabove with reference to Figs. 2–8.

[16181] VGAM1159 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16182] VGAM1159 gene, herein designated VGAM GENE, encodes a VGAM1159 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1159 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1159 precursor RNA is designated SEQ ID:30104, and is provided hereinbelow with reference to the sequence listing part.

[16183] VGAM1159 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1159 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16184] An enzyme complex designated DICER COMPLEX, dices the VGAM1159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1159 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1159 RNA is designated SEQ ID:30105, and is provided hereinbelow with reference to the sequence listing part.

[16185] VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1159 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16186] VGAM1159 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1159 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16187] The complementary binding of VGAM1159 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1159 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16188] It is appreciated that VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1159 host target genes. The mRNA of each one of this plurality of VGAM1159 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1159 RNA, herein designated VGAM RNA, and which when bound by VGAM1159 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1159 host target proteins.

[16189] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1159 gene, herein designated VGAM GENE, on one or more VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16190] It is yet further appreciated that a function of VGAM1159 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1159

correlate with, and may be deduced from, the identity of the host target genes which VGAM1159 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16191] Nucleotide sequences of the VGAM1159 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1159 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1159 are further described hereinbelow with reference to Table 1.

[16192] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1159 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16193] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1160 (VGAM1160) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[16194] VGAM1160 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1160 was detected is described hereinabove with reference to Figs. 2–8.

[16195] VGAM1160 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16196] VGAM1160 gene, herein designated VGAM GENE, encodes a VGAM1160 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1160 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1160 precursor RNA is designated SEQ ID:30143, and is provided hereinbelow with reference to the sequence listing part.

[16197] VGAM1160 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16198] An enzyme complex designated DICER COMPLEX, dices the VGAM1160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1160 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1160 RNA is designated SEQ ID:30144, and is provided hereinbelow with reference to the sequence listing part.

[16199] VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16200] VGAM1160 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1160 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1160 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16201] The complementary binding of VGAM1160 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1160 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16202] It is appreciated that VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1160 host target genes. The mRNA of each one of this plurality of VGAM1160 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1160 RNA, herein designated VGAM RNA, and which when bound by VGAM1160 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1160 host target proteins.

[16203] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1160 gene, herein designated VGAM GENE, on one or more VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16204] It is yet further appreciated that a function of VGAM1160 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1160 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM1160 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1160 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16205] Nucleotide sequences of the VGAM1160 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1160 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1160 are further described hereinbelow with reference to Table 1.

[16206] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1160 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16207] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1161 (VGAM1161) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16208] VGAM1161 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1161 was detected is described hereinabove with reference to Figs. 2–8.

[16209] VGAM1161 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16210] VGAM1161 gene, herein designated VGAM GENE, encodes a VGAM1161 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1161 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1161 precursor RNA is designated SEQ ID:30148, and is provided hereinbelow with reference to the sequence listing part.

[16211] VGAM1161 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16212] An enzyme complex designated DICER COMPLEX, dices the VGAM1161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1161 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1161 RNA is designated SEQ ID:30149, and is provided hereinbelow with reference to the sequence listing part.

[16213] VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding



gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16214] VGAM1161 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1161 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1161 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16215] The complementary binding of VGAM1161 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1161 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16216] It is appreciated that VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1161 host target genes. The mRNA of each one of this plurality of VGAM1161 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1161 RNA, herein designated VGAM RNA, and which when bound by VGAM1161 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1161 host target proteins.

[16217] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1161 gene, herein designated VGAM GENE, on one or more VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16218] It is yet further appreciated that a function of VGAM1161 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1161 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM1161 correlate with, and may be deduced from, the identity of the host target genes which VGAM1161 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[16219] Nucleotide sequences of the VGAM1161 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1161 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1161 are further described hereinbelow with reference to Table 1.

[16220] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1161 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16221] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1162 (VGAM1162) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16222] VGAM1162 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1162 was detected is described hereinabove with reference to Figs. 2–8.

[16223] VGAM1162 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum contagiosum virus. VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16224] VGAM1162 gene, herein designated VGAM GENE, encodes a VGAM1162 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1162 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1162 precursor RNA is designated SEQ ID:30153, and is provided hereinbelow with reference to the sequence listing part.

[16225] VGAM1162 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16226] An enzyme complex designated DICER COMPLEX, dices the VGAM1162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1162 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1162 RNA is designated SEQ ID:30154, and is provided hereinbelow with reference to the sequence listing part.

[16227] VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16228] VGAM1162 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1162 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[16229] The complementary binding of VGAM1162 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1162 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16230] It is appreciated that VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1162 host target genes. The mRNA of each one of this plurality of VGAM1162 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1162 RNA, herein designated VGAM RNA, and which when bound by VGAM1162 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1162 host target proteins.

[16231] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM1162 gene, herein designated VGAM GENE, on one or more VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16232] It is yet further appreciated that a function of VGAM1162 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of viral infection by Molluscum contagiosum virus. Specific functions, and accordingly utilities, of VGAM1162 correlate with, and may be deduced from, the identity of the host target genes which VGAM1162 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[16233] Nucleotide sequences of the VGAM1162 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1162 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1162 are further described hereinbelow with reference to Table 1.

[16234] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1162 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16235] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1163 (VGAM1163) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16236] VGAM1163 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1163 was detected is described hereinabove with reference to Figs. 2–8.

[16237] VGAM1163 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16238] VGAM1163 gene, herein designated VGAM GENE, encodes a VGAM1163 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1163 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1163 precursor RNA is designated SEQ ID:30160, and is provided hereinbelow with reference to the sequence listing part.

[16239] VGAM1163 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16240] An enzyme complex designated DICER COMPLEX, dices the VGAM1163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1163 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1163 RNA is designated SEQ ID:30161, and is provided hereinbelow with reference to the sequence listing part.

[16241] VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[16242] VGAM1163 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1163 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16243] The complementary binding of VGAM1163 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1163 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16244] It is appreciated that VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1163 host target genes. The mRNA of each one of this plurality of VGAM1163 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1163 RNA, herein designated VGAM RNA, and which when bound by VGAM1163 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1163 host target proteins.

[16245] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1163 gene, herein designated VGAM GENE, on one

or more VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16246] It is yet further appreciated that a function of VGAM1163 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1163 correlate with, and may be deduced from, the identity of the host target genes which VGAM1163 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16247] Nucleotide sequences of the VGAM1163 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1163 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1163 are further described hereinbelow with reference to Table 1.

[16248] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1163 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16249] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1164 (VGAM1164) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16250] VGAM1164 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1164 was detected is de-



scribed hereinabove with reference to Figs. 2–8.

[16251] VGAM1164 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1164 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16252] VGAM1164 gene, herein designated VGAM GENE, encodes a VGAM1164 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1164 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1164 precursor RNA is designated SEQ ID:30168, and is provided hereinbelow with reference to the sequence listing part.

[16253] VGAM1164 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16254] An enzyme complex designated DICER COMPLEX, dices the VGAM1164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1164 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1164 RNA is designated SEQ ID:30169, and is provided hereinbelow with reference to the sequence listing part.

[16255] VGAM1164 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16256] VGAM1164 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1164 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1164 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16257] The complementary binding of VGAM1164 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1164 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16258] It is appreciated that VGAM1164 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1164 host target genes. The mRNA of each one of this plurality of VGAM1164 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1164 RNA, herein designated VGAM RNA, and which when bound by VGAM1164 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1164 host target proteins.

[16259] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1164 gene, herein designated VGAM GENE, on one or more VGAM1164 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16260] It is yet further appreciated that a function of VGAM1164 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1164 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1164 correlate with, and may be deduced from, the identity of the host target genes which VGAM1164 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16261] Nucleotide sequences of the VGAM1164 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1164 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1164 are further described hereinbelow with reference to Table 1.

[16262] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1164 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16263] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1165 (VGAM1165) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16264] VGAM1165 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1165 was detected is described hereinabove with reference to Figs. 2-8.

[16265] VGAM1165 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16266] VGAM1165 gene, herein designated VGAM GENE, encodes a VGAM1165 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1165 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1165 precursor RNA is designated SEQ ID:30175, and is provided hereinbelow with reference to the sequence listing part.

[16267] VGAM1165 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[16268] An enzyme complex designated DICER COMPLEX, dices the VGAM1165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1165 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1165 RNA is designated SEQ ID:30176, and is provided hereinbelow with reference to the sequence listing part.

[16269] VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16270] VGAM1165 RNA, herein designated VGAM RNA, binds



complementarily to one or more host target binding sites located in untranslated regions of VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1165 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16271] The complementary binding of VGAM1165 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1165 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16272] It is appreciated that VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1165 host target genes. The mRNA of each one of this plurality of VGAM1165 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1165 RNA, herein designated VGAM RNA, and which when bound by VGAM1165 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1165 host target proteins.

[16273] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1165 gene, herein designated VGAM GENE, on one or more VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16274] It is yet further appreciated that a function of VGAM1165 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1165 correlate with, and may be deduced from, the identity of the host target genes which VGAM1165 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16275] Nucleotide sequences of the VGAM1165 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1165 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1165 are further described hereinbelow with reference to Table 1.

[16276] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1165 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16277] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1166 (VGAM1166) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16278] VGAM1166 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1166 was detected is described hereinabove with reference to Figs. 2-8.

[16279] VGAM1166 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human papillomavirus type 6. VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16280] VGAM1166 gene, herein designated VGAM GENE, encodes a VGAM1166 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1166 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1166 precursor RNA is designated SEQ ID:30182, and is provided hereinbelow with reference to the sequence listing part.

[16281] VGAM1166 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16282] An enzyme complex designated DICER COMPLEX, dices the VGAM1166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1166 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1166 RNA is designated SEQ ID:30183, and is provided hereinbelow with reference to the sequence listing part.

[16283] VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16284] VGAM1166 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1166 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1166 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16285] The complementary binding of VGAM1166 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1166 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1166 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16286] It is appreciated that VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1166 host target genes. The mRNA of each one of this plurality of VGAM1166 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1166 RNA, herein designated VGAM RNA, and which when bound by VGAM1166 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1166 host target proteins.

[16287] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1166 gene, herein designated VGAM GENE, on one or more VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16288] It is yet further appreciated that a function of VGAM1166 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1166 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 6. Specific functions, and accordingly utilities, of VGAM1166 correlate with, and may be deduced from, the identity of the host target genes which VGAM1166 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16289] Nucleotide sequences of the VGAM1166 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1166 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1166 are further described hereinbelow with reference to Table 1.

[16290] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1166 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16291] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1167 (VGAM1167) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16292] VGAM1167 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1167 was detected is described hereinabove with reference to Figs. 2-8.

[16293] VGAM1167 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus

type 6. VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16294] VGAM1167 gene, herein designated VGAM GENE, encodes a VGAM1167 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1167 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1167 precursor RNA is designated SEQ ID:30230, and is provided hereinbelow with reference to the sequence listing part.

[16295] VGAM1167 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16296] An enzyme complex designated DICER COMPLEX, dices

the VGAM1167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1167 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1167 RNA is designated SEQ ID:30231, and is provided hereinbelow with reference to the sequence listing part.

[16297] VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16298] VGAM1167 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1167 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1167 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1167 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16299] The complementary binding of VGAM1167 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1167 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16300] It is appreciated that VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1167 host target genes. The mRNA of each one of this plurality of VGAM1167 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1167 RNA, herein designated VGAM RNA, and which when bound by VGAM1167 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1167 host target proteins.

[16301] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1167 gene, herein designated VGAM GENE, on one or more VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16302] It is yet further appreciated that a function of VGAM1167 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1167 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 6. Specific functions, and accordingly utilities, of VGAM1167 correlate with, and may be deduced from, the identity of the host target genes which VGAM1167 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16303] Nucleotide sequences of the VGAM1167 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1167 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1167 are further described hereinbelow with reference to Table 1.

[16304] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1167 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16305] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1168 (VGAM1168) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16306] VGAM1168 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1168 was detected is described hereinabove with reference to Figs. 2-8.

[16307] VGAM1168 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 6. VGAM1168 host target gene, herein designated



VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16308] VGAM1168 gene, herein designated VGAM GENE, encodes a VGAM1168 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1168 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1168 precursor RNA is designated SEQ ID:30300, and is provided hereinbelow with reference to the sequence listing part.

[16309] VGAM1168 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16310] An enzyme complex designated DICER COMPLEX, dices the VGAM1168 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1168 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1168 RNA is designated SEQ ID:30301, and is provided hereinbelow with reference to the sequence listing part.

[16311] VGAM1168 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16312] VGAM1168 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1168 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1168 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16313] The complementary binding of VGAM1168 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1168

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1168 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16314] It is appreciated that VGAM1168 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1168 host target genes. The mRNA of each one of this plurality of VGAM1168 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1168 RNA, herein designated VGAM RNA, and which when bound by VGAM1168 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1168 host target proteins.

[16315] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1168 gene, herein designated VGAM GENE, on one or more VGAM1168 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16316] It is yet further appreciated that a function of VGAM1168 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1168 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 6. Specific functions, and accordingly utilities, of VGAM1168 correlate with, and may be deduced from, the identity of the host target genes which VGAM1168 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16317] Nucleotide sequences of the VGAM1168 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1168 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1168 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1168 are further described hereinbelow with reference to Table 1.

[16318] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1168 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16319] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1169 (VGAM1169) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16320] VGAM1169 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1169 was detected is described hereinabove with reference to Figs. 2-8.

[16321] VGAM1169 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1169 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[16322] VGAM1169 gene, herein designated VGAM GENE, encodes a VGAM1169 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1169 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1169 precursor RNA is designated SEQ ID:30318, and is provided hereinbelow with reference to the sequence listing part.

[16323] VGAM1169 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16324] An enzyme complex designated DICER COMPLEX, dices the VGAM1169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1169 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1169 RNA is designated SEQ ID:30319, and is provided hereinbelow with reference to the sequence listing part.

[16325] VGAM1169 host target gene, herein designated VGAM



HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16326] VGAM1169 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1169 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16327] The complementary binding of VGAM1169 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1169 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16328] It is appreciated that VGAM1169 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1169 host target genes. The mRNA of each one of this plurality of VGAM1169 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1169 RNA, herein designated VGAM

RNA, and which when bound by VGAM1169 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1169 host target proteins.

[16329] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1169 gene, herein designated VGAM GENE, on one or more VGAM1169 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16330] It is yet further appreciated that a function of VGAM1169 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1169 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM1169 correlate with, and may be deduced from, the identity of the host target genes which VGAM1169 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16331] Nucleotide sequences of the VGAM1169 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1169 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1169 are further described hereinbelow with reference to Table 1.

[16332] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1169 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16333] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1170 (VGAM1170) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16334] VGAM1170 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1170 was detected is described hereinabove with reference to Figs. 2-8.

[16335] VGAM1170 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16336] VGAM1170 gene, herein designated VGAM GENE, encodes a VGAM1170 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1170 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1170 precursor RNA is designated SEQ ID:30323, and is provided hereinbelow with reference to the sequence listing part.

[16337] VGAM1170 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16338] An enzyme complex designated DICER COMPLEX, dices the VGAM1170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1170 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1170 RNA is designated SEQ ID:30324, and is provided hereinbelow with reference to the sequence listing part.

[16339] VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16340] VGAM1170 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1170 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1170 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1170 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16341] The complementary binding of VGAM1170 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1170 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16342] It is appreciated that VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1170 host target genes. The mRNA of each one of this plurality of VGAM1170 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1170 RNA, herein designated VGAM RNA, and which when bound by VGAM1170 RNA, herein



designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1170 host target proteins.

[16343] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1170 gene, herein designated VGAM GENE, on one or more VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16344] It is yet further appreciated that a function of VGAM1170 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1170 include diagnosis, prevention and

treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM1170 correlate with, and may be deduced from, the identity of the host target genes which VGAM1170 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16345] Nucleotide sequences of the VGAM1170 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1170 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1170 are further described hereinbelow with reference to Table 1.

[16346] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1170 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16347] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1171 (VGAM1171) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16348] VGAM1171 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1171 was detected is described hereinabove with reference to Figs. 2–8.

[16349] VGAM1171 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1171 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16350] VGAM1171 gene, herein designated VGAM GENE, encodes a VGAM1171 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1171 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1171 precursor RNA is designated SEQ ID:30335, and is provided hereinbelow with reference to the sequence listing part.

[16351] VGAM1171 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1171 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16352] An enzyme complex designated DICER COMPLEX, dices the VGAM1171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1171 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1171 RNA is designated SEQ ID:30336, and is provided hereinbelow with reference to the sequence listing part.

[16353] VGAM1171 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1171 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16354] VGAM1171 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1171 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16355] The complementary binding of VGAM1171 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1171 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16356] It is appreciated that VGAM1171 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1171 host target genes. The mRNA of each one of this plurality of VGAM1171 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1171 RNA, herein designated VGAM RNA, and which when bound by VGAM1171 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1171 host target proteins.

[16357] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1171 gene, herein designated VGAM GENE, on one or more VGAM1171 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16358] It is yet further appreciated that a function of VGAM1171 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Spe-

cific functions, and accordingly utilities, of VGAM1171 correlate with, and may be deduced from, the identity of the host target genes which VGAM1171 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16359] Nucleotide sequences of the VGAM1171 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1171 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1171 are further described hereinbelow with reference to Table 1.

[16360] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1171 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16361] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1172 (VGAM1172) viral gene, which modulates expression of respective host target genes thereof, the func-



tion and utility of which host target genes is known in the art.

[16362] VGAM1172 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1172 was detected is described hereinabove with reference to Figs. 2–8.

[16363] VGAM1172 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus. VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16364] VGAM1172 gene, herein designated VGAM GENE, encodes a VGAM1172 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1172 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1172 precursor RNA is designated SEQ ID:30344, and is provided hereinbelow with reference to the sequence listing part.

[16365] VGAM1172 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1172 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16366] An enzyme complex designated DICER COMPLEX, dices the VGAM1172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1172 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1172 RNA is designated SEQ ID:30345, and is provided hereinbelow with reference to the sequence listing part.

[16367] VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1172 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16368] VGAM1172 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1172 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16369] The complementary binding of VGAM1172 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1172 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16370] It is appreciated that VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1172 host target genes. The mRNA of each one of this plurality of VGAM1172 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1172 RNA, herein designated VGAM RNA, and which when bound by VGAM1172 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1172 host target proteins.

[16371] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1172 gene, herein designated VGAM GENE, on one or more VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16372] It is yet further appreciated that a function of VGAM1172 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM1172 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1172 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16373] Nucleotide sequences of the VGAM1172 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1172 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1172 are further described hereinbelow with reference to Table 1.

[16374] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1172 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16375] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1173 (VGAM1173) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[16376] VGAM1173 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1173 was detected is described hereinabove with reference to Figs. 2–8.

[16377] VGAM1173 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus. VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16378] VGAM1173 gene, herein designated VGAM GENE, encodes a VGAM1173 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1173 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1173 precursor RNA is designated SEQ ID:30494, and is provided hereinbelow with reference to the sequence listing part.

[16379] VGAM1173 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16380] An enzyme complex designated DICER COMPLEX, dices the VGAM1173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1173 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1173 RNA is designated SEQ ID:30495, and is provided hereinbelow with reference to the sequence listing part.

[16381] VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA, comprises



three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16382] VGAM1173 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1173 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16383] The complementary binding of VGAM1173 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1173 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16384] It is appreciated that VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1173 host target genes. The mRNA of each one of this plurality of VGAM1173 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1173 RNA, herein designated VGAM RNA, and which when bound by VGAM1173 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1173 host target proteins.

[16385] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1173 gene, herein designated VGAM GENE, on one or more VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16386] It is yet further appreciated that a function of VGAM1173 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM1173 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1173 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16387] Nucleotide sequences of the VGAM1173 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1173 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1173 are further described hereinbelow with reference to Table 1.

[16388] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1173 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16389] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1174 (VGAM1174) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16390] VGAM1174 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1174 was detected is described hereinabove with reference to Figs. 2–8.

[16391] VGAM1174 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus.

VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16392] VGAM1174 gene, herein designated VGAM GENE, encodes a VGAM1174 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1174 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1174 precursor RNA is designated SEQ ID:30498, and is provided hereinbelow with reference to the sequence listing part.

[16393] VGAM1174 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16394] An enzyme complex designated DICER COMPLEX, dices the VGAM1174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1174 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1174 RNA is designated SEQ ID:30499, and is provided hereinbelow with reference to the sequence listing part.

[16395] VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16396] VGAM1174 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1174 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1174 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16397] The complementary binding of VGAM1174 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1174 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16398] It is appreciated that VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1174 host target genes. The mRNA of each one of this plurality of VGAM1174 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1174 RNA, herein designated VGAM RNA, and which when bound by VGAM1174 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1174 host target proteins.

[16399] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with



specific reference to translational inhibition exerted by VGAM1174 gene, herein designated VGAM GENE, on one or more VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16400] It is yet further appreciated that a function of VGAM1174 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1174 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM1174 correlate with, and may be deduced from, the identity of the host target genes which VGAM1174 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[16401] Nucleotide sequences of the VGAM1174 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1174 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1174 are further described hereinbelow with reference to Table 1.

[16402] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1174 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16403] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1175 (VGAM1175) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16404] VGAM1175 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1175 was detected is described hereinabove with reference to Figs. 2–8.

[16405] VGAM1175 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16406] VGAM1175 gene, herein designated VGAM GENE, encodes a VGAM1175 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1175 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1175 precursor RNA is designated SEQ ID:30503, and is provided hereinbelow with reference to the sequence listing part.

[16407] VGAM1175 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16408] An enzyme complex designated DICER COMPLEX, dices the VGAM1175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1175 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1175 RNA is designated SEQ ID:30504, and is provided hereinbelow with reference to the sequence listing part.

[16409] VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16410] VGAM1175 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1175 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1175 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[16411] The complementary binding of VGAM1175 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1175 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16412] It is appreciated that VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1175 host target genes. The mRNA of each one of this plurality of VGAM1175 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1175 RNA, herein designated VGAM RNA, and which when bound by VGAM1175 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1175 host target proteins.

[16413] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1175 gene, herein designated VGAM GENE, on one or more VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16414] It is yet further appreciated that a function of VGAM1175 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1175 correlate with, and may be deduced from, the identity of the host target genes which VGAM1175 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[16415] Nucleotide sequences of the VGAM1175 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1175 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1175 are further described hereinbelow with reference to Table 1.

[16416] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1175 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16417] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1176 (VGAM1176) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16418] VGAM1176 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.



The method by which VGAM1176 was detected is described hereinabove with reference to Figs. 2–8.

[16419] VGAM1176 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16420] VGAM1176 gene, herein designated VGAM GENE, encodes a VGAM1176 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1176 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1176 precursor RNA is designated SEQ ID:30607, and is provided hereinbelow with reference to the sequence listing part.

[16421] VGAM1176 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16422] An enzyme complex designated DICER COMPLEX, dices the VGAM1176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1176 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1176 RNA is designated SEQ ID:30608, and is provided hereinbelow with reference to the sequence listing part.

[16423] VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[16424] VGAM1176 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1176 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16425] The complementary binding of VGAM1176 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1176 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16426] It is appreciated that VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1176 host target genes. The mRNA of each one of this plurality of VGAM1176 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1176 RNA, herein designated VGAM RNA, and which when bound by VGAM1176 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1176 host target proteins.

[16427] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1176 gene, herein designated VGAM GENE, on one

or more VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16428] It is yet further appreciated that a function of VGAM1176 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM1176 correlate with, and may be deduced from, the identity of the host target genes which VGAM1176 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16429] Nucleotide sequences of the VGAM1176 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1176 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1176 are further described hereinbelow with reference to Table 1.

[16430] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1176 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16431] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1177 (VGAM1177) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16432] VGAM1177 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1177 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[16433] VGAM1177 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM1177 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16434] VGAM1177 gene, herein designated VGAM GENE, encodes a VGAM1177 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1177 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1177 precursor RNA is designated SEQ ID:30613, and is provided hereinbelow with reference to the sequence listing part.

[16435] VGAM1177 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16436] An enzyme complex designated DICER COMPLEX, dices the VGAM1177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1177 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1177 RNA is designated SEQ ID:30614, and is provided hereinbelow with reference to the sequence listing part.

[16437] VGAM1177 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.



[16438] VGAM1177 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1177 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1177 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16439] The complementary binding of VGAM1177 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1177 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16440] It is appreciated that VGAM1177 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1177 host target genes. The mRNA of each one of this plurality of VGAM1177 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1177 RNA, herein designated VGAM RNA, and which when bound by VGAM1177 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1177 host target proteins.

[16441] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1177 gene, herein designated VGAM GENE, on one or more VGAM1177 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16442] It is yet further appreciated that a function of VGAM1177 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1177 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1177 correlate with, and may be deduced from, the identity of the host target genes which VGAM1177 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16443] Nucleotide sequences of the VGAM1177 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1177 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1177 are further described hereinbelow with reference to Table 1.

[16444] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1177 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16445] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1178 (VGAM1178) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16446] VGAM1178 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1178 was detected is described hereinabove with reference to Figs. 2-8.

[16447] VGAM1178 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM1178 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16448] VGAM1178 gene, herein designated VGAM GENE, encodes a VGAM1178 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1178 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1178 precursor RNA is designated SEQ ID:30623, and is provided hereinbelow with reference to the sequence listing part.

[16449] VGAM1178 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[16450] An enzyme complex designated DICER COMPLEX, dices the VGAM1178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1178 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1178 RNA is designated SEQ ID:30624, and is provided hereinbelow with reference to the sequence listing part.

[16451] VGAM1178 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1178 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1178 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16452] VGAM1178 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1178 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1178 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1178 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1178 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16453] The complementary binding of VGAM1178 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1178 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1178 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1178 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16454] It is appreciated that VGAM1178 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1178 host target genes. The mRNA of each one of this plurality of VGAM1178 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1178 RNA, herein designated VGAM RNA, and which when bound by VGAM1178 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1178 host target proteins.

[16455] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1178 gene, herein designated VGAM GENE, on one or more VGAM1178 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other



known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16456] It is yet further appreciated that a function of VGAM1178 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1178 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1178 correlate with, and may be deduced from, the identity of the host target genes which VGAM1178 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16457] Nucleotide sequences of the VGAM1178 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1178 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1178 are further described hereinbelow with reference to Table 1.

[16458] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1178 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16459] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1179 (VGAM1179) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16460] VGAM1179 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1179 was detected is described hereinabove with reference to Figs. 2-8.

[16461] VGAM1179 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Tupaia herpesvirus. VGAM1179 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16462] VGAM1179 gene, herein designated VGAM GENE, encodes a VGAM1179 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1179 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1179 precursor RNA is designated SEQ ID:30650, and is provided hereinbelow with reference to the sequence listing part.

[16463] VGAM1179 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16464] An enzyme complex designated DICER COMPLEX, dices the VGAM1179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1179 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1179 RNA is designated SEQ ID:30651, and is provided hereinbelow with reference to the sequence listing part.

[16465] VGAM1179 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16466] VGAM1179 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1179 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1179 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16467] The complementary binding of VGAM1179 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1179 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1179 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16468] It is appreciated that VGAM1179 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1179 host target genes. The mRNA of each one of this plurality of VGAM1179 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1179 RNA, herein designated VGAM RNA, and which when bound by VGAM1179 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1179 host target proteins.

[16469] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1179 gene, herein designated VGAM GENE, on one or more VGAM1179 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16470] It is yet further appreciated that a function of VGAM1179 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1179 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1179 correlate with, and may be deduced from, the identity of the host target genes which VGAM1179 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16471] Nucleotide sequences of the VGAM1179 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1179 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1179 are further described hereinbelow with reference to Table 1.

[16472] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1179 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16473] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1180 (VGAM1180) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16474] VGAM1180 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1180 was detected is described hereinabove with reference to Figs. 2-8.

[16475] VGAM1180 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.



VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16476] VGAM1180 gene, herein designated VGAM GENE, encodes a VGAM1180 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1180 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1180 precursor RNA is designated SEQ ID:30674, and is provided hereinbelow with reference to the sequence listing part.

[16477] VGAM1180 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16478] An enzyme complex designated DICER COMPLEX, dices

the VGAM1180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1180 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1180 RNA is designated SEQ ID:30675, and is provided hereinbelow with reference to the sequence listing part.

[16479] VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16480] VGAM1180 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1180 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1180 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1180 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16481] The complementary binding of VGAM1180 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1180 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16482] It is appreciated that VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1180 host target genes. The mRNA of each one of this plurality of VGAM1180 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1180 RNA, herein designated VGAM RNA, and which when bound by VGAM1180 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1180 host target proteins.

[16483] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1180 gene, herein designated VGAM GENE, on one or more VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16484] It is yet further appreciated that a function of VGAM1180 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1180 correlate with, and may be deduced from, the identity of the host target genes which VGAM1180 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16485] Nucleotide sequences of the VGAM1180 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1180 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1180 are further described hereinbelow with reference to Table 1.

[16486] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1180 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16487] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1181 (VGAM1181) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16488] VGAM1181 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1181 was detected is described hereinabove with reference to Figs. 2-8.

[16489] VGAM1181 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1181 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[16490] VGAM1181 gene, herein designated VGAM GENE, encodes a VGAM1181 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1181 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1181 precursor RNA is designated SEQ ID:30702, and is provided hereinbelow with reference to the sequence listing part.

[16491] VGAM1181 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16492] An enzyme complex designated DICER COMPLEX, dices the VGAM1181 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1181 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1181 RNA is designated SEQ ID:30703, and is provided hereinbelow with reference to the sequence listing part.

[16493] VGAM1181 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16494] VGAM1181 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA. This



complementary binding is due to the fact that the nucleotide sequence of VGAM1181 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1181 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16495] The complementary binding of VGAM1181 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1181

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1181 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16496] It is appreciated that VGAM1181 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1181 host target genes. The mRNA of each one of this plurality of VGAM1181 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1181 RNA, herein designated VGAM RNA, and which when bound by VGAM1181 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1181 host target proteins.

[16497] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1181 gene, herein designated VGAM GENE, on one or more VGAM1181 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16498] It is yet further appreciated that a function of VGAM1181 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1181 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1181 correlate with, and may be deduced from, the identity of the host target genes which VGAM1181 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16499] Nucleotide sequences of the VGAM1181 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1181 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1181 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1181 are further described hereinbelow with reference to Table 1.

[16500] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1181 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16501] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1182 (VGAM1182) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16502] VGAM1182 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1182 was detected is described hereinabove with reference to Figs. 2-8.

[16503] VGAM1182 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[16504] VGAM1182 gene, herein designated VGAM GENE, encodes a VGAM1182 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1182 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1182 precursor RNA is designated SEQ ID:30713, and is provided hereinbelow with reference to the sequence listing part.

[16505] VGAM1182 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16506] An enzyme complex designated DICER COMPLEX, dices the VGAM1182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1182 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1182 RNA is designated SEQ ID:30714, and is provided hereinbelow with reference to the sequence listing part.

[16507] VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16508] VGAM1182 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1182 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16509] The complementary binding of VGAM1182 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1182 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1182 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16510] It is appreciated that VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1182 host target genes. The mRNA of each one of this plurality of VGAM1182 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1182 RNA, herein designated VGAM RNA, and which when bound by VGAM1182 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1182 host target proteins.

[16511] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1182 gene, herein designated VGAM GENE, on one or more VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4



and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16512] It is yet further appreciated that a function of VGAM1182 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1182 correlate with, and may be deduced from, the identity of the host target genes which VGAM1182 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16513] Nucleotide sequences of the VGAM1182 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1182 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1182 are further

described hereinbelow with reference to Table 1.

[16514] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1182 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16515] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1183 (VGAM1183) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16516] VGAM1183 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1183 was detected is described hereinabove with reference to Figs. 2-8.

[16517] VGAM1183 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16518] VGAM1183 gene, herein designated VGAM GENE, encodes a VGAM1183 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1183 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1183 precursor RNA is designated SEQ ID:30728, and is provided hereinbelow with reference to the sequence listing part.

[16519] VGAM1183 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16520] An enzyme complex designated DICER COMPLEX, dices the VGAM1183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1183 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1183 RNA is designated SEQ ID:30729, and is provided hereinbelow with reference to the sequence listing part.

[16521] VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16522] VGAM1183 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1183 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1183 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16523] The complementary binding of VGAM1183 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1183 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16524] It is appreciated that VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1183 host target genes. The mRNA of each one of this plurality of VGAM1183 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1183 RNA, herein designated VGAM RNA, and which when bound by VGAM1183 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1183 host target proteins.

[16525] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1183 gene, herein designated VGAM GENE, on one or more VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16526] It is yet further appreciated that a function of VGAM1183 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1183 correlate with, and may be deduced from, the identity of the host target genes which VGAM1183 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16527] Nucleotide sequences of the VGAM1183 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1183 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1183 are further described hereinbelow with reference to Table 1.

[16528] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1183 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16529] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1184 (VGAM1184) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16530] VGAM1184 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1184 was detected is described hereinabove with reference to Figs. 2-8.

[16531] VGAM1184 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16532] VGAM1184 gene, herein designated VGAM GENE, encodes



a VGAM1184 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1184 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1184 precursor RNA is designated SEQ ID:30824, and is provided hereinbelow with reference to the sequence listing part.

[16533] VGAM1184 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16534] An enzyme complex designated DICER COMPLEX, dices the VGAM1184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1184 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1184 RNA is designated SEQ ID:30825, and is provided hereinbelow with reference to the sequence listing part.

[16535] VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16536] VGAM1184 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1184 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1184 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16537] The complementary binding of VGAM1184 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1184 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[16538] It is appreciated that VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1184 host target genes. The mRNA of each one of this plurality of VGAM1184 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1184 RNA, herein designated VGAM RNA, and which when bound by VGAM1184 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1184 host target proteins.

[16539] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1184 gene, herein designated VGAM GENE, on one or more VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16540] It is yet further appreciated that a function of VGAM1184 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1184 correlate with, and may be deduced from, the identity of the host target genes which VGAM1184 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16541] Nucleotide sequences of the VGAM1184 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1184 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1184 are further described hereinbelow with reference to Table 1.

[16542] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1184 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16543] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1185 (VGAM1185) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16544] VGAM1185 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1185 was detected is described hereinabove with reference to Figs. 2-8.

[16545] VGAM1185 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16546] VGAM1185 gene, herein designated VGAM GENE, encodes a VGAM1185 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1185 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1185 precursor RNA is designated SEQ ID:30835, and is provided hereinbelow with reference to the sequence listing part.

[16547] VGAM1185 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16548] An enzyme complex designated DICER COMPLEX, dices the VGAM1185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1185 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1185 RNA is designated SEQ ID:30836, and is provided hereinbelow with reference to the sequence listing part.

[16549] VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16550] VGAM1185 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host



target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1185 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16551] The complementary binding of VGAM1185 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1185 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16552] It is appreciated that VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1185 host target genes. The mRNA of each one of this plurality of VGAM1185 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1185 RNA, herein designated VGAM RNA, and which when bound by VGAM1185 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1185 host target proteins.

[16553] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1185 gene, herein designated VGAM GENE, on one or more VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16554] It is yet further appreciated that a function of VGAM1185 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1185 correlate with, and may be deduced from, the identity of the host target genes which VGAM1185 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16555] Nucleotide sequences of the VGAM1185 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1185 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1185 are further described hereinbelow with reference to Table 1.

[16556] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1185 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16557] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1186 (VGAM1186) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16558] VGAM1186 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1186 was detected is described hereinabove with reference to Figs. 2-8.

[16559] VGAM1186 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 53. VGAM1186 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16560] VGAM1186 gene, herein designated VGAM GENE, encodes a VGAM1186 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1186 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1186 precursor RNA is designated SEQ ID:30842, and is provided hereinbelow with reference to the sequence listing part.

[16561] VGAM1186 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16562] An enzyme complex designated DICER COMPLEX, dices the VGAM1186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1186 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1186 RNA is designated SEQ ID:30843, and is provided hereinbelow with reference to the sequence listing part.

[16563] VGAM1186 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16564] VGAM1186 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1186 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16565] The complementary binding of VGAM1186 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1186 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16566] It is appreciated that VGAM1186 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1186 host target genes. The mRNA of each one of this plurality of VGAM1186 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1186 RNA, herein designated VGAM RNA, and which when bound by VGAM1186 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1186 host target proteins.

[16567] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1186 gene, herein designated VGAM GENE, on one or more VGAM1186 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these



other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16568] It is yet further appreciated that a function of VGAM1186 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 53. Specific functions, and accordingly utilities, of VGAM1186 correlate with, and may be deduced from, the identity of the host target genes which VGAM1186 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16569] Nucleotide sequences of the VGAM1186 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1186 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1186 are further described hereinbelow with reference to Table 1.

[16570] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1186 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16571] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1187 (VGAM1187) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16572] VGAM1187 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1187 was detected is described hereinabove with reference to Figs. 2–8.

[16573] VGAM1187 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16574] VGAM1187 gene, herein designated VGAM GENE, encodes a VGAM1187 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1187 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1187 precursor RNA is designated SEQ ID:30855, and is provided hereinbelow with reference to the sequence listing part.

[16575] VGAM1187 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16576] An enzyme complex designated DICER COMPLEX, dices the VGAM1187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1187 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1187 RNA is designated SEQ ID:30856, and is provided hereinbelow with reference to the sequence listing part.

[16577] VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16578] VGAM1187 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1187 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16579] The complementary binding of VGAM1187 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1187 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16580] It is appreciated that VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1187 host target genes. The mRNA of each one of this plurality of VGAM1187 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1187 RNA, herein designated VGAM RNA, and which when bound by VGAM1187 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1187 host target proteins.

[16581] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1187 gene, herein designated VGAM GENE, on one or more VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[16582] It is yet further appreciated that a function of VGAM1187 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM1187 correlate with, and may be deduced from, the identity of the host target genes which VGAM1187 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16583] Nucleotide sequences of the VGAM1187 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1187 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1187 are further described hereinbelow with reference to Table 1.

[16584] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1187 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16585] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1188 (VGAM1188) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16586] VGAM1188 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1188 was detected is described hereinabove with reference to Figs. 2-8.

[16587] VGAM1188 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus. VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16588] VGAM1188 gene, herein designated VGAM GENE, encodes a VGAM1188 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1188 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-



code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1188 precursor RNA is designated SEQ ID:30863, and is provided hereinbelow with reference to the sequence listing part.

[16589] VGAM1188 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16590] An enzyme complex designated DICER COMPLEX, dices the VGAM1188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1188 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM1188 RNA is designated SEQ ID:30864, and is provided hereinbelow with reference to the sequence listing part.

[16591] VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16592] VGAM1188 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1188 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16593] The complementary binding of VGAM1188 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1188 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16594] It is appreciated that VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1188 host target genes. The mRNA of

each one of this plurality of VGAM1188 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1188 RNA, herein designated VGAM RNA, and which when bound by VGAM1188 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1188 host target proteins.

[16595] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1188 gene, herein designated VGAM GENE, on one or more VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[16596] It is yet further appreciated that a function of VGAM1188 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM1188 correlate with, and may be deduced from, the identity of the host target genes which VGAM1188 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16597] Nucleotide sequences of the VGAM1188 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1188 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1188 are further described hereinbelow with reference to Table 1.

[16598] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1188 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[16599] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1189 (VGAM1189) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16600] VGAM1189 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1189 was detected is described hereinabove with reference to Figs. 2–8.

[16601] VGAM1189 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 53. VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16602] VGAM1189 gene, herein designated VGAM GENE, encodes a VGAM1189 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1189 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1189 precursor RNA is designated SEQ ID:30870, and is provided hereinbelow with reference to the sequence listing part.

[16603] VGAM1189 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16604] An enzyme complex designated DICER COMPLEX, dices the VGAM1189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1189 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1189 RNA is designated SEQ ID:30871,

and is provided hereinbelow with reference to the sequence listing part.

[16605] VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16606] VGAM1189 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites



shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1189 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16607] The complementary binding of VGAM1189 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1189 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16608] It is appreciated that VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1189 host target genes. The mRNA of each one of this plurality of VGAM1189 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1189 RNA, herein designated VGAM RNA, and which when bound by VGAM1189 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1189 host target proteins.

[16609] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1189 gene, herein designated VGAM GENE, on one or more VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16610] It is yet further appreciated that a function of VGAM1189 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 53. Specific functions, and accordingly utilities, of VGAM1189 correlate with, and may be deduced from, the identity of the host target genes which VGAM1189 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16611] Nucleotide sequences of the VGAM1189 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1189 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1189 are further described hereinbelow with reference to Table 1.

[16612] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1189 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16613] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1190 (VGAM1190) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16614] VGAM1190 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1190 was detected is described hereinabove with reference to Figs. 2–8.

[16615] VGAM1190 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 53. VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16616] VGAM1190 gene, herein designated VGAM GENE, encodes a VGAM1190 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1190 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1190 precu-

sor RNA is designated SEQ ID:30884, and is provided hereinbelow with reference to the sequence listing part.

[16617] VGAM1190 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16618] An enzyme complex designated DICER COMPLEX, dices the VGAM1190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1190 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1190 RNA is designated SEQ ID:30885, and is provided hereinbelow with reference to the se-

quence listing part.

[16619] VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16620] VGAM1190 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1190 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1190 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16621] The complementary binding of VGAM1190 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1190 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16622] It is appreciated that VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1190 host target genes. The mRNA of each one of this plurality of VGAM1190 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1190 RNA, herein designated VGAM RNA, and which when bound by VGAM1190 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1190 host target proteins.

[16623] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1190 gene, herein designated VGAM GENE, on one or more VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16624] It is yet further appreciated that a function of VGAM1190



is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1190 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 53. Specific functions, and accordingly utilities, of VGAM1190 correlate with, and may be deduced from, the identity of the host target genes which VGAM1190 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16625] Nucleotide sequences of the VGAM1190 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1190 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1190 are further described hereinbelow with reference to Table 1.

[16626] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1190 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16627] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1191 (VGAM1191) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16628] VGAM1191 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1191 was detected is described hereinabove with reference to Figs. 2–8.

[16629] VGAM1191 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16630] VGAM1191 gene, herein designated VGAM GENE, encodes a VGAM1191 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1191 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1191 precursor RNA is designated SEQ ID:30892, and is provided

hereinbelow with reference to the sequence listing part.

[16631] VGAM1191 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16632] An enzyme complex designated DICER COMPLEX, dices the VGAM1191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1191 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1191 RNA is designated SEQ ID:30893, and is provided hereinbelow with reference to the sequence listing part.

[16633] VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16634] VGAM1191 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1191 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16635] The complementary binding of VGAM1191 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1191 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16636] It is appreciated that VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1191 host target genes. The mRNA of each one of this plurality of VGAM1191 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1191 RNA, herein designated VGAM RNA, and which when bound by VGAM1191 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1191 host target proteins.

[16637] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1191 gene, herein designated VGAM GENE, on one or more VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16638] It is yet further appreciated that a function of VGAM1191 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1191 correlate with, and may be deduced from, the identity of the host target genes which VGAM1191 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16639] Nucleotide sequences of the VGAM1191 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1191 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1191 are further described hereinbelow with reference to Table 1.

[16640] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1191 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16641] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1192 (VGAM1192) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16642] VGAM1192 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1192 was detected is described hereinabove with reference to Figs. 2–8.

[16643] VGAM1192 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 30. VGAM1192 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16644] VGAM1192 gene, herein designated VGAM GENE, encodes a VGAM1192 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1192 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1192 precursor RNA is designated SEQ ID:30961, and is provided hereinbelow with reference to the sequence listing part.



[16645] VGAM1192 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16646] An enzyme complex designated DICER COMPLEX, dices the VGAM1192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1192 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1192 RNA is designated SEQ ID:30962, and is provided hereinbelow with reference to the sequence listing part.

[16647] VGAM1192 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16648] VGAM1192 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1192 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1192 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16649] The complementary binding of VGAM1192 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1192 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16650] It is appreciated that VGAM1192 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1192 host target genes. The mRNA of each one of this plurality of VGAM1192 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1192 RNA, herein designated VGAM

RNA, and which when bound by VGAM1192 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1192 host target proteins.

[16651] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1192 gene, herein designated VGAM GENE, on one or more VGAM1192 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16652] It is yet further appreciated that a function of VGAM1192 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1192 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 30. Specific functions, and accordingly utilities, of VGAM1192 correlate with, and may be deduced from, the identity of the host target genes which VGAM1192 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16653] Nucleotide sequences of the VGAM1192 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1192 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1192 are further described hereinbelow with reference to Table 1.

[16654] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1192 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16655] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1193 (VGAM1193) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16656] VGAM1193 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1193 was detected is described hereinabove with reference to Figs. 2–8.

[16657] VGAM1193 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 9. VGAM1193 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16658] VGAM1193 gene, herein designated VGAM GENE, encodes a VGAM1193 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1193 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1193 precursor RNA is designated SEQ ID:30976, and is provided hereinbelow with reference to the sequence listing part.

[16659] VGAM1193 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16660] An enzyme complex designated DICER COMPLEX, dices the VGAM1193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1193 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1193 RNA is designated SEQ ID:30977, and is provided hereinbelow with reference to the sequence listing part.

[16661] VGAM1193 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16662] VGAM1193 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1193 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1193 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1193 host



target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16663] The complementary binding of VGAM1193 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1193 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16664] It is appreciated that VGAM1193 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1193 host target genes. The mRNA of each one of this plurality of VGAM1193 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1193 RNA, herein designated VGAM RNA, and which when bound by VGAM1193 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1193 host target proteins.

[16665] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1193 gene, herein designated VGAM GENE, on one or more VGAM1193 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16666] It is yet further appreciated that a function of VGAM1193 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1193 include diagnosis, prevention and

treatment of viral infection by Human papillomavirus type 9. Specific functions, and accordingly utilities, of VGAM1193 correlate with, and may be deduced from, the identity of the host target genes which VGAM1193 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16667] Nucleotide sequences of the VGAM1193 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1193 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1193 are further described hereinbelow with reference to Table 1.

[16668] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1193 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16669] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1194 (VGAM1194) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16670] VGAM1194 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1194 was detected is described hereinabove with reference to Figs. 2–8.

[16671] VGAM1194 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 9. VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16672] VGAM1194 gene, herein designated VGAM GENE, encodes a VGAM1194 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1194 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1194 precursor RNA is designated SEQ ID:30980, and is provided hereinbelow with reference to the sequence listing part.

[16673] VGAM1194 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1194 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16674] An enzyme complex designated DICER COMPLEX, dices the VGAM1194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1194 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1194 RNA is designated SEQ ID:30981, and is provided hereinbelow with reference to the sequence listing part.

[16675] VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1194 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16676] VGAM1194 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1194 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1194 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16677] The complementary binding of VGAM1194 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1194 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16678] It is appreciated that VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1194 host target genes. The mRNA of each one of this plurality of VGAM1194 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1194 RNA, herein designated VGAM RNA, and which when bound by VGAM1194 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1194 host target proteins.

[16679] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1194 gene, herein designated VGAM GENE, on one or more VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16680] It is yet further appreciated that a function of VGAM1194 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type



9. Specific functions, and accordingly utilities, of VGAM1194 correlate with, and may be deduced from, the identity of the host target genes which VGAM1194 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16681] Nucleotide sequences of the VGAM1194 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1194 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1194 are further described hereinbelow with reference to Table 1.

[16682] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1194 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16683] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1195 (VGAM1195) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[16684] VGAM1195 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1195 was detected is described hereinabove with reference to Figs. 2–8.

[16685] VGAM1195 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 30. VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16686] VGAM1195 gene, herein designated VGAM GENE, encodes a VGAM1195 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1195 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1195 precursor RNA is designated SEQ ID:30987, and is provided hereinbelow with reference to the sequence listing part.

[16687] VGAM1195 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1195 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16688] An enzyme complex designated DICER COMPLEX, dices the VGAM1195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1195 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1195 RNA is designated SEQ ID:30988, and is provided hereinbelow with reference to the sequence listing part.

[16689] VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1195 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16690] VGAM1195 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1195 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16691] The complementary binding of VGAM1195 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1195 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16692] It is appreciated that VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1195 host target genes. The mRNA of each one of this plurality of VGAM1195 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1195 RNA, herein designated VGAM RNA, and which when bound by VGAM1195 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1195 host target proteins.

[16693] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1195 gene, herein designated VGAM GENE, on one or more VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16694] It is yet further appreciated that a function of VGAM1195 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 30. Specific functions, and accordingly utilities, of

VGAM1195 correlate with, and may be deduced from, the identity of the host target genes which VGAM1195 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16695] Nucleotide sequences of the VGAM1195 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1195 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1195 are further described hereinbelow with reference to Table 1.

[16696] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1195 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16697] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1196 (VGAM1196) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[16698] VGAM1196 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1196 was detected is described hereinabove with reference to Figs. 2–8.

[16699] VGAM1196 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 30. VGAM1196 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16700] VGAM1196 gene, herein designated VGAM GENE, encodes a VGAM1196 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1196 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1196 precursor RNA is designated SEQ ID:30999, and is provided hereinbelow with reference to the sequence listing part.

[16701] VGAM1196 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.



As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16702] An enzyme complex designated DICER COMPLEX, dices the VGAM1196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1196 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1196 RNA is designated SEQ ID:31000, and is provided hereinbelow with reference to the sequence listing part.

[16703] VGAM1196 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16704] VGAM1196 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1196 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1196 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16705] The complementary binding of VGAM1196 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1196 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16706] It is appreciated that VGAM1196 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1196 host target genes. The mRNA of each one of this plurality of VGAM1196 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1196 RNA, herein designated VGAM RNA, and which when bound by VGAM1196 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1196 host target proteins.

[16707] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1196 gene, herein designated VGAM GENE, on one or more VGAM1196 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16708] It is yet further appreciated that a function of VGAM1196 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1196 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 30. Specific functions, and accordingly utilities, of VGAM1196 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1196 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16709] Nucleotide sequences of the VGAM1196 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1196 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1196 are further described hereinbelow with reference to Table 1.

[16710] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1196 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16711] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1197 (VGAM1197) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16712] VGAM1197 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1197 was detected is described hereinabove with reference to Figs. 2–8.

[16713] VGAM1197 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 30. VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16714] VGAM1197 gene, herein designated VGAM GENE, encodes a VGAM1197 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1197 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1197 precursor RNA is designated SEQ ID:31009, and is provided hereinbelow with reference to the sequence listing part.

[16715] VGAM1197 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16716] An enzyme complex designated DICER COMPLEX, dices the VGAM1197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1197 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1197 RNA is designated SEQ ID:31010, and is provided hereinbelow with reference to the sequence listing part.

[16717] VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16718] VGAM1197 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1197 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-



cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16719] The complementary binding of VGAM1197 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1197 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16720] It is appreciated that VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1197 host target genes. The mRNA of each one of this plurality of VGAM1197 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1197 RNA, herein designated VGAM RNA, and which when bound by VGAM1197 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1197 host target proteins.

[16721] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1197 gene, herein designated VGAM GENE, on one or more VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16722] It is yet further appreciated that a function of VGAM1197 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 30. Specific functions, and accordingly utilities, of VGAM1197 correlate with, and may be deduced from, the identity of the host target genes which VGAM1197 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16723] Nucleotide sequences of the VGAM1197 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1197 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1197 are further described hereinbelow with reference to Table 1.

[16724] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1197 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16725] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1198 (VGAM1198) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16726] VGAM1198 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1198 was detected is described hereinabove with reference to Figs. 2–8.

[16727] VGAM1198 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 30. VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16728] VGAM1198 gene, herein designated VGAM GENE, encodes a VGAM1198 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1198 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1198 precursor RNA is designated SEQ ID:31012, and is provided hereinbelow with reference to the sequence listing part.

[16729] VGAM1198 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16730] An enzyme complex designated DICER COMPLEX, dices the VGAM1198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1198 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1198 RNA is designated SEQ ID:31013, and is provided hereinbelow with reference to the sequence listing part.

[16731] VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16732] VGAM1198 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1198 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1198 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[16733] The complementary binding of VGAM1198 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1198 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16734] It is appreciated that VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1198 host target genes. The mRNA of each one of this plurality of VGAM1198 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1198 RNA, herein designated VGAM RNA, and which when bound by VGAM1198 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1198 host target proteins.

[16735] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1198 gene, herein designated VGAM GENE, on one or more VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16736] It is yet further appreciated that a function of VGAM1198 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1198 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 30. Specific functions, and accordingly utilities, of VGAM1198 correlate with, and may be deduced from, the identity of the host target genes which VGAM1198 binds and inhibits, and the function of these host target genes,



as elaborated hereinbelow.

[16737] Nucleotide sequences of the VGAM1198 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1198 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1198 are further described hereinbelow with reference to Table 1.

[16738] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1198 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16739] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1199 (VGAM1199) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16740] VGAM1199 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1199 was detected is described hereinabove with reference to Figs. 2–8.

[16741] VGAM1199 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria hypovirus 3. VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16742] VGAM1199 gene, herein designated VGAM GENE, encodes a VGAM1199 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1199 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1199 precursor RNA is designated SEQ ID:31017, and is provided hereinbelow with reference to the sequence listing part.

[16743] VGAM1199 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16744] An enzyme complex designated DICER COMPLEX, dices the VGAM1199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1199 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1199 RNA is designated SEQ ID:31018, and is provided hereinbelow with reference to the sequence listing part.

[16745] VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[16746] VGAM1199 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1199 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1199 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16747] The complementary binding of VGAM1199 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1199 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16748] It is appreciated that VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1199 host target genes. The mRNA of each one of this plurality of VGAM1199 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1199 RNA, herein designated VGAM RNA, and which when bound by VGAM1199 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1199 host target proteins.

[16749] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1199 gene, herein designated VGAM GENE, on one

or more VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16750] It is yet further appreciated that a function of VGAM1199 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1199 include diagnosis, prevention and treatment of viral infection by Cryphonectria hypovirus 3. Specific functions, and accordingly utilities, of VGAM1199 correlate with, and may be deduced from, the identity of the host target genes which VGAM1199 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16751] Nucleotide sequences of the VGAM1199 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1199 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1199 are further described hereinbelow with reference to Table 1.

[16752] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1199 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16753] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1200 (VGAM1200) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16754] VGAM1200 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1200 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[16755] VGAM1200 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8.

VGAM1200 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16756] VGAM1200 gene, herein designated VGAM GENE, encodes a VGAM1200 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1200 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1200 precursor RNA is designated SEQ ID:31109, and is provided hereinbelow with reference to the sequence listing part.

[16757] VGAM1200 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial



inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16758] An enzyme complex designated DICER COMPLEX, dices the VGAM1200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1200 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1200 RNA is designated SEQ ID:31110, and is provided hereinbelow with reference to the sequence listing part.

[16759] VGAM1200 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16760] VGAM1200 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1200 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16761] The complementary binding of VGAM1200 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1200 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16762] It is appreciated that VGAM1200 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1200 host target genes. The mRNA of each one of this plurality of VGAM1200 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1200 RNA, herein designated VGAM RNA, and which when bound by VGAM1200 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1200 host target proteins.

[16763] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1200 gene, herein designated VGAM GENE, on one or more VGAM1200 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16764] It is yet further appreciated that a function of VGAM1200 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1200 correlate with, and may be deduced from, the identity of the host target genes which VGAM1200 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16765] Nucleotide sequences of the VGAM1200 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1200 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1200 are further described hereinbelow with reference to Table 1.

[16766] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1200 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16767] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1201 (VGAM1201) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16768] VGAM1201 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1201 was detected is described hereinabove with reference to Figs. 2-8.

[16769] VGAM1201 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16770] VGAM1201 gene, herein designated VGAM GENE, encodes a VGAM1201 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1201 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1201 precursor RNA is designated SEQ ID:31113, and is provided hereinbelow with reference to the sequence listing part.

[16771] VGAM1201 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[16772] An enzyme complex designated DICER COMPLEX, dices the VGAM1201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1201 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1201 RNA is designated SEQ ID:31114, and is provided hereinbelow with reference to the sequence listing part.

[16773] VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16774] VGAM1201 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1201 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16775] The complementary binding of VGAM1201 RNA, herein designated VGAM RNA, to host target binding sites on



VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1201 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16776] It is appreciated that VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1201 host target genes. The mRNA of each one of this plurality of VGAM1201 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1201 RNA, herein designated VGAM RNA, and which when bound by VGAM1201 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1201 host target proteins.

[16777] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1201 gene, herein designated VGAM GENE, on one or more VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16778] It is yet further appreciated that a function of VGAM1201 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1201 correlate with, and may be deduced from, the identity of the host target genes which VGAM1201 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16779] Nucleotide sequences of the VGAM1201 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1201 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1201 are further described hereinbelow with reference to Table 1.

[16780] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1201 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16781] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1202 (VGAM1202) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16782] VGAM1202 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1202 was detected is described hereinabove with reference to Figs. 2-8.

[16783] VGAM1202 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 8. VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16784] VGAM1202 gene, herein designated VGAM GENE, encodes a VGAM1202 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1202 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1202 precursor RNA is designated SEQ ID:31142, and is provided hereinbelow with reference to the sequence listing part.

[16785] VGAM1202 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16786] An enzyme complex designated DICER COMPLEX, dices the VGAM1202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1202 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1202 RNA is designated SEQ ID:31143, and is provided hereinbelow with reference to the sequence listing part.

[16787] VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16788] VGAM1202 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1202 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1202 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16789] The complementary binding of VGAM1202 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1202 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1202 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16790] It is appreciated that VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1202 host target genes. The mRNA of each one of this plurality of VGAM1202 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1202 RNA, herein designated VGAM RNA, and which when bound by VGAM1202 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1202 host target proteins.

[16791] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1202 gene, herein designated VGAM GENE, on one or more VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16792] It is yet further appreciated that a function of VGAM1202 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1202 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1202 correlate with, and may be deduced from, the identity of the host target genes which VGAM1202 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16793] Nucleotide sequences of the VGAM1202 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1202 RNA, herein designated VGAM RNA, and



a schematic representation of the secondary folding of VGAM1202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1202 are further described hereinbelow with reference to Table 1.

[16794] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1202 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16795] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1203 (VGAM1203) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16796] VGAM1203 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1203 was detected is described hereinabove with reference to Figs. 2-8.

[16797] VGAM1203 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus

type 26. VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16798] VGAM1203 gene, herein designated VGAM GENE, encodes a VGAM1203 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1203 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1203 precursor RNA is designated SEQ ID:31148, and is provided hereinbelow with reference to the sequence listing part.

[16799] VGAM1203 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16800] An enzyme complex designated DICER COMPLEX, dices

the VGAM1203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1203 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1203 RNA is designated SEQ ID:31149, and is provided hereinbelow with reference to the sequence listing part.

[16801] VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16802] VGAM1203 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1203 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1203 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1203 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16803] The complementary binding of VGAM1203 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1203 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16804] It is appreciated that VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1203 host target genes. The mRNA of each one of this plurality of VGAM1203 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1203 RNA, herein designated VGAM RNA, and which when bound by VGAM1203 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1203 host target proteins.

[16805] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1203 gene, herein designated VGAM GENE, on one or more VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16806] It is yet further appreciated that a function of VGAM1203 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1203 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 26. Specific functions, and accordingly utilities, of VGAM1203 correlate with, and may be deduced from, the identity of the host target genes which VGAM1203 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16807] Nucleotide sequences of the VGAM1203 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1203 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1203 are further described hereinbelow with reference to Table 1.

[16808] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1203 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16809] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1204 (VGAM1204) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16810] VGAM1204 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1204 was detected is described hereinabove with reference to Figs. 2-8.

[16811] VGAM1204 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM1204 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[16812] VGAM1204 gene, herein designated VGAM GENE, encodes a VGAM1204 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1204 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1204 precursor RNA is designated SEQ ID:31309, and is provided hereinbelow with reference to the sequence listing part.

[16813] VGAM1204 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16814] An enzyme complex designated DICER COMPLEX, dices the VGAM1204 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, into VGAM1204 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1204 RNA is designated SEQ ID:31310, and is provided hereinbelow with reference to the sequence listing part.

[16815] VGAM1204 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16816] VGAM1204 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1204 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16817] The complementary binding of VGAM1204 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1204

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1204 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16818] It is appreciated that VGAM1204 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1204 host target genes. The mRNA of each one of this plurality of VGAM1204 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1204 RNA, herein designated VGAM RNA, and which when bound by VGAM1204 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1204 host target proteins.

[16819] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1204 gene, herein designated VGAM GENE, on one or more VGAM1204 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16820] It is yet further appreciated that a function of VGAM1204 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1204 correlate with, and may be deduced from, the identity of the host target genes which VGAM1204 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16821] Nucleotide sequences of the VGAM1204 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1204 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1204 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1204 are further described hereinbelow with reference to Table 1.

[16822] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1204 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16823] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1205 (VGAM1205) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16824] VGAM1205 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1205 was detected is described hereinabove with reference to Figs. 2-8.

[16825] VGAM1205 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[16826] VGAM1205 gene, herein designated VGAM GENE, encodes a VGAM1205 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1205 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1205 precursor RNA is designated SEQ ID:31357, and is provided hereinbelow with reference to the sequence listing part.

[16827] VGAM1205 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16828] An enzyme complex designated DICER COMPLEX, dices the VGAM1205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1205 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1205 RNA is designated SEQ ID:31358, and is provided hereinbelow with reference to the sequence listing part.

[16829] VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16830] VGAM1205 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1205 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16831] The complementary binding of VGAM1205 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1205 host target RNA, herein designated VGAM HOST TARGET



RNA, into VGAM1205 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16832] It is appreciated that VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1205 host target genes. The mRNA of each one of this plurality of VGAM1205 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1205 RNA, herein designated VGAM RNA, and which when bound by VGAM1205 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1205 host target proteins.

[16833] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1205 gene, herein designated VGAM GENE, on one or more VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16834] It is yet further appreciated that a function of VGAM1205 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1205 correlate with, and may be deduced from, the identity of the host target genes which VGAM1205 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16835] Nucleotide sequences of the VGAM1205 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1205 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1205 are further

described hereinbelow with reference to Table 1.

[16836] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1205 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16837] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1206 (VGAM1206) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16838] VGAM1206 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1206 was detected is described hereinabove with reference to Figs. 2-8.

[16839] VGAM1206 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16840] VGAM1206 gene, herein designated VGAM GENE, encodes a VGAM1206 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1206 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1206 precursor RNA is designated SEQ ID:31364, and is provided hereinbelow with reference to the sequence listing part.

[16841] VGAM1206 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16842] An enzyme complex designated DICER COMPLEX, dices the VGAM1206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1206 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1206 RNA is designated SEQ ID:31365, and is provided hereinbelow with reference to the sequence listing part.

[16843] VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16844] VGAM1206 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1206 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1206 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16845] The complementary binding of VGAM1206 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1206 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16846] It is appreciated that VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1206 host target genes. The mRNA of each one of this plurality of VGAM1206 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1206 RNA, herein designated VGAM RNA, and which when bound by VGAM1206 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1206 host target proteins.

[16847] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1206 gene, herein designated VGAM GENE, on one or more VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16848] It is yet further appreciated that a function of VGAM1206 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1206 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1206 correlate with, and may be deduced from, the identity of the host target genes which VGAM1206 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16849] Nucleotide sequences of the VGAM1206 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1206 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1206 are further described hereinbelow with reference to Table 1.



[16850] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1206 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16851] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1207 (VGAM1207) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16852] VGAM1207 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1207 was detected is described hereinabove with reference to Figs. 2-8.

[16853] VGAM1207 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM1207 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16854] VGAM1207 gene, herein designated VGAM GENE, encodes

a VGAM1207 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1207 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1207 precursor RNA is designated SEQ ID:31394, and is provided hereinbelow with reference to the sequence listing part.

[16855] VGAM1207 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16856] An enzyme complex designated DICER COMPLEX, dices the VGAM1207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1207 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1207 RNA is designated SEQ ID:31395, and is provided hereinbelow with reference to the sequence listing part.

[16857] VGAM1207 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16858] VGAM1207 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1207 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1207 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16859] The complementary binding of VGAM1207 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1207 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[16860] It is appreciated that VGAM1207 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1207 host target genes. The mRNA of each one of this plurality of VGAM1207 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1207 RNA, herein designated VGAM RNA, and which when bound by VGAM1207 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1207 host target proteins.

[16861] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1207 gene, herein designated VGAM GENE, on one or more VGAM1207 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16862] It is yet further appreciated that a function of VGAM1207 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1207 correlate with, and may be deduced from, the identity of the host target genes which VGAM1207 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16863] Nucleotide sequences of the VGAM1207 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1207 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1207 are further described hereinbelow with reference to Table 1.

[16864] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1207 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16865] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1208 (VGAM1208) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16866] VGAM1208 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1208 was detected is described hereinabove with reference to Figs. 2-8.

[16867] VGAM1208 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16868] VGAM1208 gene, herein designated VGAM GENE, encodes a VGAM1208 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1208 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1208 precursor RNA is designated SEQ ID:31432, and is provided hereinbelow with reference to the sequence listing part.

[16869] VGAM1208 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16870] An enzyme complex designated DICER COMPLEX, dices the VGAM1208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1208 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short



~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1208 RNA is designated SEQ ID:31433, and is provided hereinbelow with reference to the sequence listing part.

[16871] VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16872] VGAM1208 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1208 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16873] The complementary binding of VGAM1208 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1208 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16874] It is appreciated that VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1208 host target genes. The mRNA of each one of this plurality of VGAM1208 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1208 RNA, herein designated VGAM RNA, and which when bound by VGAM1208 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1208 host target proteins.

[16875] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1208 gene, herein designated VGAM GENE, on one or more VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16876] It is yet further appreciated that a function of VGAM1208 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1208 correlate with, and may be deduced from, the identity of the host target genes which VGAM1208 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16877] Nucleotide sequences of the VGAM1208 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1208 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1208 are further described hereinbelow with reference to Table 1.

[16878] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1208 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16879] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1209 (VGAM1209) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16880] VGAM1209 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1209 was detected is described hereinabove with reference to Figs. 2-8.

[16881] VGAM1209 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 45. VGAM1209 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16882] VGAM1209 gene, herein designated VGAM GENE, encodes a VGAM1209 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1209 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1209 precursor RNA is designated SEQ ID:31461, and is provided hereinbelow with reference to the sequence listing part.

[16883] VGAM1209 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16884] An enzyme complex designated DICER COMPLEX, dices the VGAM1209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1209 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1209 RNA is designated SEQ ID:31462, and is provided hereinbelow with reference to the sequence listing part.

[16885] VGAM1209 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16886] VGAM1209 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1209 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16887] The complementary binding of VGAM1209 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1209 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16888] It is appreciated that VGAM1209 host target gene, herein



designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1209 host target genes. The mRNA of each one of this plurality of VGAM1209 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1209 RNA, herein designated VGAM RNA, and which when bound by VGAM1209 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1209 host target proteins.

[16889] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1209 gene, herein designated VGAM GENE, on one or more VGAM1209 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16890] It is yet further appreciated that a function of VGAM1209 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 45. Specific functions, and accordingly utilities, of VGAM1209 correlate with, and may be deduced from, the identity of the host target genes which VGAM1209 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16891] Nucleotide sequences of the VGAM1209 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1209 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1209 are further described hereinbelow with reference to Table 1.

[16892] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1209 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16893] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1210 (VGAM1210) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16894] VGAM1210 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1210 was detected is described hereinabove with reference to Figs. 2–8.

[16895] VGAM1210 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16896] VGAM1210 gene, herein designated VGAM GENE, encodes a VGAM1210 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1210 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1210 precursor RNA is designated SEQ ID:31479, and is provided hereinbelow with reference to the sequence listing part.

[16897] VGAM1210 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16898] An enzyme complex designated DICER COMPLEX, dices the VGAM1210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1210 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1210 RNA is designated SEQ ID:31480, and is provided hereinbelow with reference to the sequence listing part.

[16899] VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16900] VGAM1210 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1210 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16901] The complementary binding of VGAM1210 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1210 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16902] It is appreciated that VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1210 host target genes. The mRNA of each one of this plurality of VGAM1210 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1210 RNA, herein designated VGAM RNA, and which when bound by VGAM1210 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1210 host target proteins.

[16903] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1210 gene, herein designated VGAM GENE, on one or more VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[16904] It is yet further appreciated that a function of VGAM1210 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1210 correlate with, and may be deduced from, the identity of the host target genes which VGAM1210 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16905] Nucleotide sequences of the VGAM1210 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1210 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1210 are further described hereinbelow with reference to Table 1.

[16906] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites



to VGAM1210 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16907] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1211 (VGAM1211) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16908] VGAM1211 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1211 was detected is described hereinabove with reference to Figs. 2-8.

[16909] VGAM1211 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16910] VGAM1211 gene, herein designated VGAM GENE, encodes a VGAM1211 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1211 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1211 precursor RNA is designated SEQ ID:31512, and is provided hereinbelow with reference to the sequence listing part.

[16911] VGAM1211 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16912] An enzyme complex designated DICER COMPLEX, dices the VGAM1211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1211 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1211 RNA is designated SEQ ID:31513, and is provided hereinbelow with reference to the sequence listing part.

[16913] VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16914] VGAM1211 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1211 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1211 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16915] The complementary binding of VGAM1211 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1211 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16916] It is appreciated that VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1211 host target genes. The mRNA of

each one of this plurality of VGAM1211 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1211 RNA, herein designated VGAM RNA, and which when bound by VGAM1211 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1211 host target proteins.

[16917] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1211 gene, herein designated VGAM GENE, on one or more VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[16918] It is yet further appreciated that a function of VGAM1211 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1211 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1211 correlate with, and may be deduced from, the identity of the host target genes which VGAM1211 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16919] Nucleotide sequences of the VGAM1211 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1211 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1211 are further described hereinbelow with reference to Table 1.

[16920] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1211 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[16921] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1212 (VGAM1212) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16922] VGAM1212 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1212 was detected is described hereinabove with reference to Figs. 2–8.

[16923] VGAM1212 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM1212 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16924] VGAM1212 gene, herein designated VGAM GENE, encodes a VGAM1212 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1212 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1212 precursor RNA is designated SEQ ID:31527, and is provided hereinbelow with reference to the sequence listing part.

[16925] VGAM1212 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16926] An enzyme complex designated DICER COMPLEX, dices the VGAM1212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1212 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1212 RNA is designated SEQ ID:31433,



and is provided hereinbelow with reference to the sequence listing part.

[16927] VGAM1212 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16928] VGAM1212 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1212 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1212 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16929] The complementary binding of VGAM1212 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1212 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16930] It is appreciated that VGAM1212 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1212 host target genes. The mRNA of each one of this plurality of VGAM1212 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1212 RNA, herein designated VGAM RNA, and which when bound by VGAM1212 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1212 host target proteins.

[16931] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1212 gene, herein designated VGAM GENE, on one or more VGAM1212 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16932] It is yet further appreciated that a function of VGAM1212 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1212 correlate with, and may be deduced from, the identity of the host target genes which VGAM1212 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16933] Nucleotide sequences of the VGAM1212 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1212 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1212 are further described hereinbelow with reference to Table 1.

[16934] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1212 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16935] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1213 (VGAM1213) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16936] VGAM1213 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1213 was detected is described hereinabove with reference to Figs. 2–8.

[16937] VGAM1213 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 45. VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16938] VGAM1213 gene, herein designated VGAM GENE, encodes a VGAM1213 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1213 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1213 precursor

sor RNA is designated SEQ ID:31528, and is provided hereinbelow with reference to the sequence listing part.

[16939] VGAM1213 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16940] An enzyme complex designated DICER COMPLEX, dices the VGAM1213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1213 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1213 RNA is designated SEQ ID:31529, and is provided hereinbelow with reference to the se-

quence listing part.

[16941] VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16942] VGAM1213 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1213 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1213 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16943] The complementary binding of VGAM1213 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1213 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16944] It is appreciated that VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1213 host target genes. The mRNA of each one of this plurality of VGAM1213 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1213 RNA, herein designated VGAM RNA, and which when bound by VGAM1213 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1213 host target proteins.

[16945] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1213 gene, herein designated VGAM GENE, on one or more VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16946] It is yet further appreciated that a function of VGAM1213

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1213 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 45. Specific functions, and accordingly utilities, of VGAM1213 correlate with, and may be deduced from, the identity of the host target genes which VGAM1213 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16947] Nucleotide sequences of the VGAM1213 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1213 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1213 are further described hereinbelow with reference to Table 1.

[16948] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1213 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16949] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1214 (VGAM1214) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16950] VGAM1214 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1214 was detected is described hereinabove with reference to Figs. 2–8.

[16951] VGAM1214 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16952] VGAM1214 gene, herein designated VGAM GENE, encodes a VGAM1214 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1214 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1214 precursor RNA is designated SEQ ID:31551, and is provided

hereinbelow with reference to the sequence listing part.

[16953] VGAM1214 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16954] An enzyme complex designated DICER COMPLEX, dices the VGAM1214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1214 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1214 RNA is designated SEQ ID:31552, and is provided hereinbelow with reference to the sequence listing part.

[16955] VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16956] VGAM1214 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1214 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16957] The complementary binding of VGAM1214 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1214 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16958] It is appreciated that VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1214 host target genes. The mRNA of each one of this plurality of VGAM1214 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1214 RNA, herein designated VGAM RNA, and which when bound by VGAM1214 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1214 host target proteins.

[16959] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1214 gene, herein designated VGAM GENE, on one or more VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16960] It is yet further appreciated that a function of VGAM1214 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1214 correlate with, and may be deduced from, the identity of the host target genes which VGAM1214 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16961] Nucleotide sequences of the VGAM1214 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1214 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1214 are further described hereinbelow with reference to Table 1.

[16962] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1214 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16963]

[16964] Fig. 1 further provides a conceptual description of a novel



bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1215 (VGAM1215) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16965] VGAM1215 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1215 was detected is described hereinabove with reference to Figs. 2–8.

[16966] VGAM1215 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM1215 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16967] VGAM1215 gene, herein designated VGAM GENE, encodes a VGAM1215 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1215 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1215 precursor RNA is designated SEQ ID:31559, and is provided hereinbelow with reference to the sequence listing part.

[16968] VGAM1215 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16969] An enzyme complex designated DICER COMPLEX, dices the VGAM1215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1215 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1215 RNA is designated SEQ ID:31560, and is provided hereinbelow with reference to the sequence listing part.

[16970] VGAM1215 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16971] VGAM1215 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1215 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1215 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16972] The complementary binding of VGAM1215 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1215 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16973] It is appreciated that VGAM1215 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1215 host target genes. The mRNA of each one of this plurality of VGAM1215 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1215 RNA, herein designated VGAM

RNA, and which when bound by VGAM1215 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1215 host target proteins.

[16974] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1215 gene, herein designated VGAM GENE, on one or more VGAM1215 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16975] It is yet further appreciated that a function of VGAM1215 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1215 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1.

Specific functions, and accordingly utilities, of VGAM1215 correlate with, and may be deduced from, the identity of the host target genes which VGAM1215 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16976] Nucleotide sequences of the VGAM1215 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1215 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1215 are further described hereinbelow with reference to Table 1.

[16977] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1215 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16978] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1216 (VGAM1216) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16979] VGAM1216 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1216 was detected is described hereinabove with reference to Figs. 2-8.

[16980] VGAM1216 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16981] VGAM1216 gene, herein designated VGAM GENE, encodes a VGAM1216 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1216 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1216 precursor RNA is designated SEQ ID:31565, and is provided hereinbelow with reference to the sequence listing part.

[16982] VGAM1216 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16983] An enzyme complex designated DICER COMPLEX, dices the VGAM1216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1216 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1216 RNA is designated SEQ ID:31566, and is provided hereinbelow with reference to the sequence listing part.

[16984] VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16985] VGAM1216 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1216 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1216 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[16986] The complementary binding of VGAM1216 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1216 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16987] It is appreciated that VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1216 host target genes. The mRNA of each one of this plurality of VGAM1216 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1216 RNA, herein designated VGAM RNA, and which when bound by VGAM1216 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1216 host target proteins.

[16988] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1216 gene, herein designated VGAM GENE, on one or more VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[16989] It is yet further appreciated that a function of VGAM1216 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1216 include diagnosis, prevention and

treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1216 correlate with, and may be deduced from, the identity of the host target genes which VGAM1216 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16990] Nucleotide sequences of the VGAM1216 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1216 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1216 are further described hereinbelow with reference to Table 1.

[16991] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1216 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16992] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1217 (VGAM1217) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16993] VGAM1217 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1217 was detected is described hereinabove with reference to Figs. 2–8.

[16994] VGAM1217 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16995] VGAM1217 gene, herein designated VGAM GENE, encodes a VGAM1217 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1217 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1217 precursor RNA is designated SEQ ID:31578, and is provided hereinbelow with reference to the sequence listing part.

[16996] VGAM1217 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1217 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16997] An enzyme complex designated DICER COMPLEX, dices the VGAM1217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1217 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1217 RNA is designated SEQ ID:31579, and is provided hereinbelow with reference to the sequence listing part.

[16998] VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1217 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[16999] VGAM1217 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1217 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17000] The complementary binding of VGAM1217 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1217 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17001] It is appreciated that VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1217 host target genes. The mRNA of each one of this plurality of VGAM1217 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1217 RNA, herein designated VGAM RNA, and which when bound by VGAM1217 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM1217 host target proteins.

[17002] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1217 gene, herein designated VGAM GENE, on one or more VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17003] It is yet further appreciated that a function of VGAM1217 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1.

Specific functions, and accordingly utilities, of VGAM1217 correlate with, and may be deduced from, the identity of the host target genes which VGAM1217 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17004] Nucleotide sequences of the VGAM1217 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1217 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1217 are further described hereinbelow with reference to Table 1.

[17005] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1217 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17006] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1218 (VGAM1218) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[17007] VGAM1218 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1218 was detected is described hereinabove with reference to Figs. 2–8.

[17008] VGAM1218 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1218 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17009] VGAM1218 gene, herein designated VGAM GENE, encodes a VGAM1218 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1218 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1218 precursor RNA is designated SEQ ID:31603, and is provided hereinbelow with reference to the sequence listing part.

[17010] VGAM1218 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1218 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17011] An enzyme complex designated DICER COMPLEX, dices the VGAM1218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1218 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1218 RNA is designated SEQ ID:31604, and is provided hereinbelow with reference to the sequence listing part.

[17012] VGAM1218 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1218 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17013] VGAM1218 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1218 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1218 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17014] The complementary binding of VGAM1218 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1218 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17015] It is appreciated that VGAM1218 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1218 host target genes. The mRNA of each one of this plurality of VGAM1218 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1218 RNA, herein designated VGAM RNA, and which when bound by VGAM1218 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1218 host target proteins.

[17016] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1218 gene, herein designated VGAM GENE, on one or more VGAM1218 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17017] It is yet further appreciated that a function of VGAM1218 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1218 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1218

correlate with, and may be deduced from, the identity of the host target genes which VGAM1218 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17018] Nucleotide sequences of the VGAM1218 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1218 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1218 are further described hereinbelow with reference to Table 1.

[17019] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1218 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17020] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1219 (VGAM1219) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[17021] VGAM1219 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1219 was detected is described hereinabove with reference to Figs. 2–8.

[17022] VGAM1219 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17023] VGAM1219 gene, herein designated VGAM GENE, encodes a VGAM1219 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1219 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1219 precursor RNA is designated SEQ ID:31611, and is provided hereinbelow with reference to the sequence listing part.

[17024] VGAM1219 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17025] An enzyme complex designated DICER COMPLEX, dices the VGAM1219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1219 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1219 RNA is designated SEQ ID:31612, and is provided hereinbelow with reference to the sequence listing part.

[17026] VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17027] VGAM1219 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1219 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1219 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17028] The complementary binding of VGAM1219 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1219 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17029] It is appreciated that VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1219 host target genes. The mRNA of each one of this plurality of VGAM1219 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1219 RNA, herein designated VGAM RNA, and which when bound by VGAM1219 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1219 host target proteins.

[17030] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1219 gene, herein designated VGAM GENE, on one or more VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17031] It is yet further appreciated that a function of VGAM1219 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1219 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1219 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1219 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17032] Nucleotide sequences of the VGAM1219 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1219 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1219 are further described hereinbelow with reference to Table 1.

[17033] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1219 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17034] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1220 (VGAM1220) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17035] VGAM1220 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1220 was detected is described hereinabove with reference to Figs. 2–8.

[17036] VGAM1220 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17037] VGAM1220 gene, herein designated VGAM GENE, encodes a VGAM1220 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1220 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1220 precursor RNA is designated SEQ ID:31621, and is provided hereinbelow with reference to the sequence listing part.

[17038] VGAM1220 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17039] An enzyme complex designated DICER COMPLEX, dices the VGAM1220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1220 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1220 RNA is designated SEQ ID:31622, and is provided hereinbelow with reference to the sequence listing part.

[17040] VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding



gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17041] VGAM1220 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1220 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17042] The complementary binding of VGAM1220 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1220 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17043] It is appreciated that VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1220 host target genes. The mRNA of each one of this plurality of VGAM1220 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1220 RNA, herein designated VGAM RNA, and which when bound by VGAM1220 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1220 host target proteins.

[17044] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1220 gene, herein designated VGAM GENE, on one or more VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17045] It is yet further appreciated that a function of VGAM1220 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1220 correlate with, and may be deduced from, the identity of the host target genes which VGAM1220 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[17046] Nucleotide sequences of the VGAM1220 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1220 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1220 are further described hereinbelow with reference to Table 1.

[17047] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1220 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17048] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1221 (VGAM1221) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17049] VGAM1221 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1221 was detected is described hereinabove with reference to Figs. 2–8.

[17050] VGAM1221 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17051] VGAM1221 gene, herein designated VGAM GENE, encodes a VGAM1221 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1221 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1221 precursor RNA is designated SEQ ID:31629, and is provided hereinbelow with reference to the sequence listing part.

[17052] VGAM1221 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17053] An enzyme complex designated DICER COMPLEX, dices the VGAM1221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1221 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1221 RNA is designated SEQ ID:31630, and is provided hereinbelow with reference to the sequence listing part.

[17054] VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17055] VGAM1221 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1221 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[17056] The complementary binding of VGAM1221 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1221 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17057] It is appreciated that VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1221 host target genes. The mRNA of each one of this plurality of VGAM1221 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1221 RNA, herein designated VGAM RNA, and which when bound by VGAM1221 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1221 host target proteins.

[17058] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM1221 gene, herein designated VGAM GENE, on one or more VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17059] It is yet further appreciated that a function of VGAM1221 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1221 correlate with, and may be deduced from, the identity of the host target genes which VGAM1221 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[17060] Nucleotide sequences of the VGAM1221 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1221 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1221 are further described hereinbelow with reference to Table 1.

[17061] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1221 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17062] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1222 (VGAM1222) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17063] VGAM1222 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1222 was detected is described hereinabove with reference to Figs. 2–8.

[17064] VGAM1222 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid herpesvirus 1. VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17065] VGAM1222 gene, herein designated VGAM GENE, encodes a VGAM1222 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1222 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1222 precursor RNA is designated SEQ ID:31644, and is provided hereinbelow with reference to the sequence listing part.

[17066] VGAM1222 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17067] An enzyme complex designated DICER COMPLEX, dices the VGAM1222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1222 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1222 RNA is designated SEQ ID:31645, and is provided hereinbelow with reference to the sequence listing part.

[17068] VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[17069] VGAM1222 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1222 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1222 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17070] The complementary binding of VGAM1222 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1222 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17071] It is appreciated that VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1222 host target genes. The mRNA of each one of this plurality of VGAM1222 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1222 RNA, herein designated VGAM RNA, and which when bound by VGAM1222 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1222 host target proteins.

[17072] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1222 gene, herein designated VGAM GENE, on one

or more VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17073] It is yet further appreciated that a function of VGAM1222 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1222 include diagnosis, prevention and treatment of viral infection by Ictalurid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1222 correlate with, and may be deduced from, the identity of the host target genes which VGAM1222 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17074] Nucleotide sequences of the VGAM1222 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1222 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1222 are further described hereinbelow with reference to Table 1.

[17075] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1222 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17076] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1223 (VGAM1223) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17077] VGAM1223 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1223 was detected is de-



scribed hereinabove with reference to Figs. 2–8.

[17078] VGAM1223 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1223 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17079] VGAM1223 gene, herein designated VGAM GENE, encodes a VGAM1223 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1223 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1223 precursor RNA is designated SEQ ID:31650, and is provided hereinbelow with reference to the sequence listing part.

[17080] VGAM1223 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17081] An enzyme complex designated DICER COMPLEX, dices the VGAM1223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1223 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1223 RNA is designated SEQ ID:31651, and is provided hereinbelow with reference to the sequence listing part.

[17082] VGAM1223 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17083] VGAM1223 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1223 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17084] The complementary binding of VGAM1223 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1223 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17085] It is appreciated that VGAM1223 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1223 host target genes. The mRNA of each one of this plurality of VGAM1223 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1223 RNA, herein designated VGAM RNA, and which when bound by VGAM1223 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1223 host target proteins.

[17086] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1223 gene, herein designated VGAM GENE, on one or more VGAM1223 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17087] It is yet further appreciated that a function of VGAM1223 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1223 correlate with, and may be deduced from, the identity of the host target genes which VGAM1223 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17088] Nucleotide sequences of the VGAM1223 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1223 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1223 are further described hereinbelow with reference to Table 1.

[17089] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1223 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17090] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1224 (VGAM1224) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17091] VGAM1224 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1224 was detected is described hereinabove with reference to Figs. 2-8.

[17092] VGAM1224 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhesus monkey papillomavirus. VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17093] VGAM1224 gene, herein designated VGAM GENE, encodes a VGAM1224 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1224 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1224 precursor RNA is designated SEQ ID:31658, and is provided hereinbelow with reference to the sequence listing part.

[17094] VGAM1224 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[17095] An enzyme complex designated DICER COMPLEX, dices the VGAM1224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1224 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1224 RNA is designated SEQ ID:31659, and is provided hereinbelow with reference to the sequence listing part.

[17096] VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17097] VGAM1224 RNA, herein designated VGAM RNA, binds



complementarily to one or more host target binding sites located in untranslated regions of VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1224 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17098] The complementary binding of VGAM1224 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1224 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17099] It is appreciated that VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1224 host target genes. The mRNA of each one of this plurality of VGAM1224 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1224 RNA, herein designated VGAM RNA, and which when bound by VGAM1224 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1224 host target proteins.

[17100] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1224 gene, herein designated VGAM GENE, on one or more VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17101] It is yet further appreciated that a function of VGAM1224 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of viral infection by Rhesus monkey papillomavirus. Specific functions, and accordingly utilities, of VGAM1224 correlate with, and may be deduced from, the identity of the host target genes which VGAM1224 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17102] Nucleotide sequences of the VGAM1224 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1224 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1224 are further described hereinbelow with reference to Table 1.

[17103] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1224 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17104] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1225 (VGAM1225) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17105] VGAM1225 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1225 was detected is described hereinabove with reference to Figs. 2-8.

[17106] VGAM1225 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Rhesus monkey papillomavirus. VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17107] VGAM1225 gene, herein designated VGAM GENE, encodes a VGAM1225 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1225 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1225 precursor RNA is designated SEQ ID:31690, and is provided hereinbelow with reference to the sequence listing part.

[17108] VGAM1225 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17109] An enzyme complex designated DICER COMPLEX, dices the VGAM1225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1225 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1225 RNA is designated SEQ ID:31691, and is provided hereinbelow with reference to the sequence listing part.

[17110] VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17111] VGAM1225 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1225 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17112] The complementary binding of VGAM1225 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1225 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1225 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17113] It is appreciated that VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1225 host target genes. The mRNA of each one of this plurality of VGAM1225 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1225 RNA, herein designated VGAM RNA, and which when bound by VGAM1225 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1225 host target proteins.

[17114] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1225 gene, herein designated VGAM GENE, on one or more VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17115] It is yet further appreciated that a function of VGAM1225 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of viral infection by Rhesus monkey papillomavirus. Specific functions, and accordingly utilities, of VGAM1225 correlate with, and may be deduced from, the identity of the host target genes which VGAM1225 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17116] Nucleotide sequences of the VGAM1225 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1225 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1225 are further described hereinbelow with reference to Table 1.

[17117] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1225 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17118] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1226 (VGAM1226) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17119] VGAM1226 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1226 was detected is described hereinabove with reference to Figs. 2-8.

[17120] VGAM1226 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine her-

pesvirus 7. VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17121] VGAM1226 gene, herein designated VGAM GENE, encodes a VGAM1226 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1226 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1226 precursor RNA is designated SEQ ID:31702, and is provided hereinbelow with reference to the sequence listing part.

[17122] VGAM1226 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17123] An enzyme complex designated DICER COMPLEX, dices

the VGAM1226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1226 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1226 RNA is designated SEQ ID:31703, and is provided hereinbelow with reference to the sequence listing part.

[17124] VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17125] VGAM1226 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1226 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1226 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17126] The complementary binding of VGAM1226 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1226 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17127] It is appreciated that VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1226 host target genes. The mRNA of each one of this plurality of VGAM1226 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1226 RNA, herein designated VGAM RNA, and which when bound by VGAM1226 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1226 host target proteins.

[17128] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1226 gene, herein designated VGAM GENE, on one or more VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17129] It is yet further appreciated that a function of VGAM1226 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1226 correlate with, and may be deduced from, the identity of the host target genes which VGAM1226 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17130] Nucleotide sequences of the VGAM1226 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1226 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1226 are further described hereinbelow with reference to Table 1.

[17131] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1226 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17132] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1227 (VGAM1227) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17133] VGAM1227 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1227 was detected is described hereinabove with reference to Figs. 2-8.

[17134] VGAM1227 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhesus monkey papillomavirus. VGAM1227 host target gene, herein designated



VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17135] VGAM1227 gene, herein designated VGAM GENE, encodes a VGAM1227 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1227 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1227 precursor RNA is designated SEQ ID:31720, and is provided hereinbelow with reference to the sequence listing part.

[17136] VGAM1227 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17137] An enzyme complex designated DICER COMPLEX, dices the VGAM1227 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1227 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1227 RNA is designated SEQ ID:31721, and is provided hereinbelow with reference to the sequence listing part.

[17138] VGAM1227 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17139] VGAM1227 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1227 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1227 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17140] The complementary binding of VGAM1227 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1227

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1227 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17141] It is appreciated that VGAM1227 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1227 host target genes. The mRNA of each one of this plurality of VGAM1227 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1227 RNA, herein designated VGAM RNA, and which when bound by VGAM1227 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1227 host target proteins.

[17142] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1227 gene, herein designated VGAM GENE, on one or more VGAM1227 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17143] It is yet further appreciated that a function of VGAM1227 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1227 include diagnosis, prevention and treatment of viral infection by Rhesus monkey papillomavirus. Specific functions, and accordingly utilities, of VGAM1227 correlate with, and may be deduced from, the identity of the host target genes which VGAM1227 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17144] Nucleotide sequences of the VGAM1227 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1227 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1227 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1227 are further described hereinbelow with reference to Table 1.

[17145] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1227 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17146] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1228 (VGAM1228) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17147] VGAM1228 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1228 was detected is described hereinabove with reference to Figs. 2-8.

[17148] VGAM1228 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhesus monkey papillomavirus. VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[17149] VGAM1228 gene, herein designated VGAM GENE, encodes a VGAM1228 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1228 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1228 precursor RNA is designated SEQ ID:31728, and is provided hereinbelow with reference to the sequence listing part.

[17150] VGAM1228 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17151] An enzyme complex designated DICER COMPLEX, dices the VGAM1228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1228 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1228 RNA is designated SEQ ID:31729, and is provided hereinbelow with reference to the sequence listing part.

[17152] VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17153] VGAM1228 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1228 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17154] The complementary binding of VGAM1228 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1228 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1228 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17155] It is appreciated that VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1228 host target genes. The mRNA of each one of this plurality of VGAM1228 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1228 RNA, herein designated VGAM RNA, and which when bound by VGAM1228 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1228 host target proteins.

[17156] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1228 gene, herein designated VGAM GENE, on one or more VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17157] It is yet further appreciated that a function of VGAM1228 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of viral infection by Rhesus monkey papillomavirus. Specific functions, and accordingly utilities, of VGAM1228 correlate with, and may be deduced from, the identity of the host target genes which VGAM1228 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17158] Nucleotide sequences of the VGAM1228 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1228 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1228 are further

described hereinbelow with reference to Table 1.

[17159] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1228 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17160] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1229 (VGAM1229) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17161] VGAM1229 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1229 was detected is described hereinabove with reference to Figs. 2-8.

[17162] VGAM1229 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17163] VGAM1229 gene, herein designated VGAM GENE, encodes a VGAM1229 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1229 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1229 precursor RNA is designated SEQ ID:31759, and is provided hereinbelow with reference to the sequence listing part.

[17164] VGAM1229 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17165] An enzyme complex designated DICER COMPLEX, dices the VGAM1229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1229 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1229 RNA is designated SEQ ID:31760, and is provided hereinbelow with reference to the sequence listing part.

[17166] VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17167] VGAM1229 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1229 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1229 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17168] The complementary binding of VGAM1229 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1229 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17169] It is appreciated that VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1229 host target genes. The mRNA of each one of this plurality of VGAM1229 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1229 RNA, herein designated VGAM RNA, and which when bound by VGAM1229 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1229 host target proteins.

[17170] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1229 gene, herein designated VGAM GENE, on one or more VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17171] It is yet further appreciated that a function of VGAM1229 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1229 correlate with, and may be deduced from, the identity of the host target genes which VGAM1229 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17172] Nucleotide sequences of the VGAM1229 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1229 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1229 are further described hereinbelow with reference to Table 1.

[17173] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1229 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17174] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1230 (VGAM1230) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17175] VGAM1230 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1230 was detected is described hereinabove with reference to Figs. 2-8.

[17176] VGAM1230 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhesus monkey papillomavirus. VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17177] VGAM1230 gene, herein designated VGAM GENE, encodes

a VGAM1230 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1230 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1230 precursor RNA is designated SEQ ID:31765, and is provided hereinbelow with reference to the sequence listing part.

[17178] VGAM1230 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17179] An enzyme complex designated DICER COMPLEX, dices the VGAM1230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1230 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1230 RNA is designated SEQ ID:31766, and is provided hereinbelow with reference to the sequence listing part.

[17180] VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17181] VGAM1230 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1230 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17182] The complementary binding of VGAM1230 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1230 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[17183] It is appreciated that VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1230 host target genes. The mRNA of each one of this plurality of VGAM1230 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1230 RNA, herein designated VGAM RNA, and which when bound by VGAM1230 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1230 host target proteins.

[17184] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1230 gene, herein designated VGAM GENE, on one or more VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17185] It is yet further appreciated that a function of VGAM1230 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of viral infection by Rhesus monkey papillomavirus. Specific functions, and accordingly utilities, of VGAM1230 correlate with, and may be deduced from, the identity of the host target genes which VGAM1230 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17186] Nucleotide sequences of the VGAM1230 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1230 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1230 are further described hereinbelow with reference to Table 1.

[17187] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1230 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17188] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1231 (VGAM1231) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17189] VGAM1231 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1231 was detected is described hereinabove with reference to Figs. 2-8.

[17190] VGAM1231 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 66. VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17191] VGAM1231 gene, herein designated VGAM GENE, encodes a VGAM1231 precursor RNA, herein designated VGAM



PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1231 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1231 precursor RNA is designated SEQ ID:31773, and is provided hereinbelow with reference to the sequence listing part.

[17192] VGAM1231 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17193] An enzyme complex designated DICER COMPLEX, dices the VGAM1231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1231 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1231 RNA is designated SEQ ID:31774, and is provided hereinbelow with reference to the sequence listing part.

[17194] VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17195] VGAM1231 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1231 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17196] The complementary binding of VGAM1231 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1231 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17197] It is appreciated that VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1231 host target genes. The mRNA of each one of this plurality of VGAM1231 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1231 RNA, herein designated VGAM RNA, and which when bound by VGAM1231 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1231 host target proteins.

[17198] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1231 gene, herein designated VGAM GENE, on one or more VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17199] It is yet further appreciated that a function of VGAM1231 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 66. Specific functions, and accordingly utilities, of VGAM1231 correlate with, and may be deduced from, the identity of the host target genes which VGAM1231 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17200] Nucleotide sequences of the VGAM1231 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1231 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1231 are further described hereinbelow with reference to Table 1.

[17201] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1231 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17202] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1232 (VGAM1232) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17203] VGAM1232 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1232 was detected is described hereinabove with reference to Figs. 2-8.

[17204] VGAM1232 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM1232 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17205] VGAM1232 gene, herein designated VGAM GENE, encodes a VGAM1232 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1232 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1232 precursor RNA is designated SEQ ID:31801, and is provided hereinbelow with reference to the sequence listing part.

[17206] VGAM1232 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17207] An enzyme complex designated DICER COMPLEX, dices the VGAM1232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1232 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1232 RNA is designated SEQ ID:31802, and is provided hereinbelow with reference to the sequence listing part.

[17208] VGAM1232 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17209] VGAM1232 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1232 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1232 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17210] The complementary binding of VGAM1232 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1232 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17211] It is appreciated that VGAM1232 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1232 host target genes. The mRNA of each one of this plurality of VGAM1232 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1232 RNA, herein designated VGAM RNA, and which when bound by VGAM1232 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1232 host target proteins.

[17212] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1232 gene, herein designated VGAM GENE, on one or more VGAM1232 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17213] It is yet further appreciated that a function of VGAM1232 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1232 correlate with, and may be deduced from, the identity of the host target genes which VGAM1232 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17214] Nucleotide sequences of the VGAM1232 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1232 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1232 are further described hereinbelow with reference to Table 1.

[17215] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1232 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17216] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1233 (VGAM1233) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17217] VGAM1233 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1233 was detected is described hereinabove with reference to Figs. 2–8.

[17218] VGAM1233 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 66. VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17219] VGAM1233 gene, herein designated VGAM GENE, encodes a VGAM1233 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1233 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1233 precursor RNA is designated SEQ ID:31810, and is provided hereinbelow with reference to the sequence listing part.

[17220] VGAM1233 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17221] An enzyme complex designated DICER COMPLEX, dices the VGAM1233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1233 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1233 RNA is designated SEQ ID:31811, and is provided hereinbelow with reference to the sequence listing part.

[17222] VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17223] VGAM1233 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1233 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17224] The complementary binding of VGAM1233 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1233 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17225] It is appreciated that VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1233 host target genes. The mRNA of each one of this plurality of VGAM1233 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1233 RNA, herein designated VGAM RNA, and which when bound by VGAM1233 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1233 host target proteins.

[17226] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1233 gene, herein designated VGAM GENE, on one or more VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[17227] It is yet further appreciated that a function of VGAM1233 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 66. Specific functions, and accordingly utilities, of VGAM1233 correlate with, and may be deduced from, the identity of the host target genes which VGAM1233 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17228] Nucleotide sequences of the VGAM1233 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1233 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1233 are further described hereinbelow with reference to Table 1.

[17229] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1233 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17230] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1234 (VGAM1234) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17231] VGAM1234 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1234 was detected is described hereinabove with reference to Figs. 2-8.

[17232] VGAM1234 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17233] VGAM1234 gene, herein designated VGAM GENE, encodes a VGAM1234 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1234 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1234 precursor RNA is designated SEQ ID:31823, and is provided hereinbelow with reference to the sequence listing part.

[17234] VGAM1234 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17235] An enzyme complex designated DICER COMPLEX, dices the VGAM1234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1234 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1234 RNA is designated SEQ ID:31824, and is provided hereinbelow with reference to the sequence listing part.

[17236] VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17237] VGAM1234 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1234 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17238] The complementary binding of VGAM1234 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1234 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17239] It is appreciated that VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1234 host target genes. The mRNA of

each one of this plurality of VGAM1234 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1234 RNA, herein designated VGAM RNA, and which when bound by VGAM1234 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1234 host target proteins.

[17240] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1234 gene, herein designated VGAM GENE, on one or more VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[17241] It is yet further appreciated that a function of VGAM1234 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1234 correlate with, and may be deduced from, the identity of the host target genes which VGAM1234 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17242] Nucleotide sequences of the VGAM1234 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1234 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1234 are further described hereinbelow with reference to Table 1.

[17243] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1234 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[17244] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1235 (VGAM1235) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17245] VGAM1235 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1235 was detected is described hereinabove with reference to Figs. 2–8.

[17246] VGAM1235 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian foamy virus. VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17247] VGAM1235 gene, herein designated VGAM GENE, encodes a VGAM1235 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1235 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly



similar to the nucleotide sequence of VGAM1235 precursor RNA is designated SEQ ID:31834, and is provided hereinbelow with reference to the sequence listing part.

[17248] VGAM1235 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17249] An enzyme complex designated DICER COMPLEX, dices the VGAM1235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1235 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1235 RNA is designated SEQ ID:31835,

and is provided hereinbelow with reference to the sequence listing part.

[17250] VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17251] VGAM1235 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1235 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17252] The complementary binding of VGAM1235 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1235 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17253] It is appreciated that VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1235 host target genes. The mRNA of each one of this plurality of VGAM1235 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1235 RNA, herein designated VGAM RNA, and which when bound by VGAM1235 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1235 host target proteins.

[17254] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1235 gene, herein designated VGAM GENE, on one or more VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17255] It is yet further appreciated that a function of VGAM1235 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of viral infection by Simian foamy virus. Specific functions, and accordingly utilities, of VGAM1235 correlate with, and may be deduced from, the identity of the host target genes which VGAM1235 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17256] Nucleotide sequences of the VGAM1235 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1235 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1235 are further described hereinbelow with reference to Table 1.

[17257] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1235 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17258] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1236 (VGAM1236) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17259] VGAM1236 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1236 was detected is described hereinabove with reference to Figs. 2–8.

[17260] VGAM1236 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17261] VGAM1236 gene, herein designated VGAM GENE, encodes a VGAM1236 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1236 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1236 precu-

sor RNA is designated SEQ ID:31841, and is provided hereinbelow with reference to the sequence listing part.

[17262] VGAM1236 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17263] An enzyme complex designated DICER COMPLEX, dices the VGAM1236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1236 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1236 RNA is designated SEQ ID:31842, and is provided hereinbelow with reference to the se-

quence listing part.

[17264] VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17265] VGAM1236 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1236 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM1236 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17266] The complementary binding of VGAM1236 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1236 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17267] It is appreciated that VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1236 host target genes. The mRNA of each one of this plurality of VGAM1236 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1236 RNA, herein designated VGAM RNA, and which when bound by VGAM1236 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1236 host target proteins.

[17268] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1236 gene, herein designated VGAM GENE, on one or more VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17269] It is yet further appreciated that a function of VGAM1236

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1236 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1236 correlate with, and may be deduced from, the identity of the host target genes which VGAM1236 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17270] Nucleotide sequences of the VGAM1236 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1236 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1236 are further described hereinbelow with reference to Table 1.

[17271] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1236 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17272] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1237 (VGAM1237) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17273] VGAM1237 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1237 was detected is described hereinabove with reference to Figs. 2–8.

[17274] VGAM1237 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Periplaneta fuliginosa* densovirus. VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17275] VGAM1237 gene, herein designated VGAM GENE, encodes a VGAM1237 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1237 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1237 precursor RNA is designated SEQ ID:31865, and is provided

hereinbelow with reference to the sequence listing part.

[17276] VGAM1237 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17277] An enzyme complex designated DICER COMPLEX, dices the VGAM1237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1237 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 100%) nucleotide sequence of VGAM1237 RNA is designated SEQ ID:31866, and is provided hereinbelow with reference to the sequence listing part.

[17278] VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17279] VGAM1237 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1237 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17280] The complementary binding of VGAM1237 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1237 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17281] It is appreciated that VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1237 host target genes. The mRNA of each one of this plurality of VGAM1237 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1237 RNA, herein designated VGAM RNA, and which when bound by VGAM1237 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1237 host target proteins.

[17282] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1237 gene, herein designated VGAM GENE, on one or more VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17283] It is yet further appreciated that a function of VGAM1237 is inhibition of expression of host target genes, as part of



a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of viral infection by *Periplaneta fuliginosa* densovirus. Specific functions, and accordingly utilities, of VGAM1237 correlate with, and may be deduced from, the identity of the host target genes which VGAM1237 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17284] Nucleotide sequences of the VGAM1237 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1237 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1237 are further described hereinbelow with reference to Table 1.

[17285] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1237 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17286] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1238 (VGAM1238) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17287] VGAM1238 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1238 was detected is described hereinabove with reference to Figs. 2–8.

[17288] VGAM1238 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian foamy virus. VGAM1238 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17289] VGAM1238 gene, herein designated VGAM GENE, encodes a VGAM1238 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1238 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1238 precursor RNA is designated SEQ ID:31877, and is provided hereinbelow with reference to the sequence listing part.

[17290] VGAM1238 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17291] An enzyme complex designated DICER COMPLEX, dices the VGAM1238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1238 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1238 RNA is designated SEQ ID:31878, and is provided hereinbelow with reference to the sequence listing part.

[17292] VGAM1238 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17293] VGAM1238 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1238 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17294] The complementary binding of VGAM1238 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1238 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17295] It is appreciated that VGAM1238 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1238 host target genes. The mRNA of each one of this plurality of VGAM1238 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1238 RNA, herein designated VGAM

RNA, and which when bound by VGAM1238 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1238 host target proteins.

[17296] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1238 gene, herein designated VGAM GENE, on one or more VGAM1238 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17297] It is yet further appreciated that a function of VGAM1238 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1238 include diagnosis, prevention and treatment of viral infection by Simian foamy virus. Specific functions, and accordingly utilities, of VGAM1238 correlate with, and may be deduced from, the identity of the host target genes which VGAM1238 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17298] Nucleotide sequences of the VGAM1238 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1238 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1238 are further described hereinbelow with reference to Table 1.

[17299] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1238 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17300] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1239 (VGAM1239) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17301] VGAM1239 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1239 was detected is described hereinabove with reference to Figs. 2-8.

[17302] VGAM1239 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian foamy virus. VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17303] VGAM1239 gene, herein designated VGAM GENE, encodes a VGAM1239 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1239 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1239 precursor RNA is designated SEQ ID:31897, and is provided hereinbelow with reference to the sequence listing part.

[17304] VGAM1239 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM1239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17305] An enzyme complex designated DICER COMPLEX, dices the VGAM1239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1239 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1239 RNA is designated SEQ ID:31898, and is provided hereinbelow with reference to the sequence listing part.

[17306] VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17307] VGAM1239 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1239 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1239 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17308] The complementary binding of VGAM1239 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1239 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17309] It is appreciated that VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1239 host target genes. The mRNA of each one of this plurality of VGAM1239 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1239 RNA, herein designated VGAM RNA, and which when bound by VGAM1239 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1239 host target proteins.

[17310] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1239 gene, herein designated VGAM GENE, on one or more VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17311] It is yet further appreciated that a function of VGAM1239 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1239 include diagnosis, prevention and

treatment of viral infection by Simian foamy virus. Specific functions, and accordingly utilities, of VGAM1239 correlate with, and may be deduced from, the identity of the host target genes which VGAM1239 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17312] Nucleotide sequences of the VGAM1239 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1239 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1239 are further described hereinbelow with reference to Table 1.

[17313] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1239 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17314] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1240 (VGAM1240) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17315] VGAM1240 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1240 was detected is described hereinabove with reference to Figs. 2–8.

[17316] VGAM1240 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian foamy virus. VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17317] VGAM1240 gene, herein designated VGAM GENE, encodes a VGAM1240 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1240 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1240 precursor RNA is designated SEQ ID:31916, and is provided hereinbelow with reference to the sequence listing part.

[17318] VGAM1240 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1240 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17319] An enzyme complex designated DICER COMPLEX, dices the VGAM1240 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1240 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1240 RNA is designated SEQ ID:31917, and is provided hereinbelow with reference to the sequence listing part.

[17320] VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1240 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17321] VGAM1240 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1240 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17322] The complementary binding of VGAM1240 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1240 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17323] It is appreciated that VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1240 host target genes. The mRNA of each one of this plurality of VGAM1240 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1240 RNA, herein designated VGAM RNA, and which when bound by VGAM1240 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1240 host target proteins.

[17324] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1240 gene, herein designated VGAM GENE, on one or more VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17325] It is yet further appreciated that a function of VGAM1240 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of viral infection by Simian foamy virus. Specific

functions, and accordingly utilities, of VGAM1240 correlate with, and may be deduced from, the identity of the host target genes which VGAM1240 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17326] Nucleotide sequences of the VGAM1240 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1240 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1240 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1240 are further described hereinbelow with reference to Table 1.

[17327] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1240 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17328] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1241 (VGAM1241) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[17329] VGAM1241 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1241 was detected is described hereinabove with reference to Figs. 2–8.

[17330] VGAM1241 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian foamy virus. VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17331] VGAM1241 gene, herein designated VGAM GENE, encodes a VGAM1241 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1241 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1241 precursor RNA is designated SEQ ID:31921, and is provided hereinbelow with reference to the sequence listing part.

[17332] VGAM1241 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1241 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17333] An enzyme complex designated DICER COMPLEX, dices the VGAM1241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1241 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1241 RNA is designated SEQ ID:31922, and is provided hereinbelow with reference to the sequence listing part.

[17334] VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1241 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17335] VGAM1241 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1241 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1241 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17336] The complementary binding of VGAM1241 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1241 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17337] It is appreciated that VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1241 host target genes. The mRNA of each one of this plurality of VGAM1241 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1241 RNA, herein designated VGAM RNA, and which when bound by VGAM1241 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1241 host target proteins.

[17338] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1241 gene, herein designated VGAM GENE, on one or more VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17339] It is yet further appreciated that a function of VGAM1241 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1241 include diagnosis, prevention and treatment of viral infection by Simian foamy virus. Specific functions, and accordingly utilities, of VGAM1241 corre-



late with, and may be deduced from, the identity of the host target genes which VGAM1241 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17340] Nucleotide sequences of the VGAM1241 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1241 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1241 are further described hereinbelow with reference to Table 1.

[17341] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1241 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17342] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1242 (VGAM1242) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17343] VGAM1242 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1242 was detected is described hereinabove with reference to Figs. 2–8.

[17344] VGAM1242 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17345] VGAM1242 gene, herein designated VGAM GENE, encodes a VGAM1242 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1242 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1242 precursor

sor RNA is designated SEQ ID:31939, and is provided hereinbelow with reference to the sequence listing part.

[17346] VGAM1242 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17347] An enzyme complex designated DICER COMPLEX, dices the VGAM1242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1242 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1242 RNA is designated SEQ ID:31940, and is provided hereinbelow with reference to the se-

quence listing part.

[17348] VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17349] VGAM1242 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1242 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17350] The complementary binding of VGAM1242 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1242 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17351] It is appreciated that VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1242 host target genes. The mRNA of each one of this plurality of VGAM1242 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1242 RNA, herein designated VGAM RNA, and which when bound by VGAM1242 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1242 host target proteins.

[17352] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1242 gene, herein designated VGAM GENE, on one or more VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17353] It is yet further appreciated that a function of VGAM1242

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1242 correlate with, and may be deduced from, the identity of the host target genes which VGAM1242 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17354] Nucleotide sequences of the VGAM1242 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1242 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1242 are further described hereinbelow with reference to Table 1.

[17355] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1242 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17356] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1243 (VGAM1243) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17357] VGAM1243 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1243 was detected is described hereinabove with reference to Figs. 2–8.

[17358] VGAM1243 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 3. VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17359] VGAM1243 gene, herein designated VGAM GENE, encodes a VGAM1243 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1243 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1243 precursor RNA is designated SEQ ID:31956, and is provided



hereinbelow with reference to the sequence listing part.

[17360] VGAM1243 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17361] An enzyme complex designated DICER COMPLEX, dices the VGAM1243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1243 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1243 RNA is designated SEQ ID:31957, and is provided hereinbelow with reference to the sequence listing part.

[17362] VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17363] VGAM1243 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1243 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1243 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17364] The complementary binding of VGAM1243 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1243 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17365] It is appreciated that VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1243 host target genes. The mRNA of each one of this plurality of VGAM1243 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1243 RNA, herein designated VGAM RNA, and which when bound by VGAM1243 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1243 host target proteins.

[17366] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1243 gene, herein designated VGAM GENE, on one or more VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17367] It is yet further appreciated that a function of VGAM1243 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1243 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1243 correlate with, and may be deduced from, the identity of the host target genes which VGAM1243 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17368] Nucleotide sequences of the VGAM1243 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1243 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1243 are further described hereinbelow with reference to Table 1.

[17369] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1243 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17370] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1244 (VGAM1244) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17371] VGAM1244 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1244 was detected is described hereinabove with reference to Figs. 2–8.

[17372] VGAM1244 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1244 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17373] VGAM1244 gene, herein designated VGAM GENE, encodes a VGAM1244 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1244 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1244 precursor RNA is designated SEQ ID:31968, and is provided hereinbelow with reference to the sequence listing part.

[17374] VGAM1244 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17375] An enzyme complex designated DICER COMPLEX, dices the VGAM1244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1244 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1244 RNA is designated SEQ ID:31969, and is provided hereinbelow with reference to the sequence listing part.

[17376] VGAM1244 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17377] VGAM1244 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1244 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1244 RNA, herein designated VGAM RNA, may have a different number of host target



binding sites in untranslated regions of a VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17378] The complementary binding of VGAM1244 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1244 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17379] It is appreciated that VGAM1244 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1244 host target genes. The mRNA of each one of this plurality of VGAM1244 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1244 RNA, herein designated VGAM

RNA, and which when bound by VGAM1244 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1244 host target proteins.

[17380] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1244 gene, herein designated VGAM GENE, on one or more VGAM1244 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17381] It is yet further appreciated that a function of VGAM1244 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1244 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1244 correlate with, and may be deduced from, the identity of the host target genes which VGAM1244 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17382] Nucleotide sequences of the VGAM1244 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1244 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1244 are further described hereinbelow with reference to Table 1.

[17383] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1244 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17384] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1245 (VGAM1245) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17385] VGAM1245 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1245 was detected is described hereinabove with reference to Figs. 2-8.

[17386] VGAM1245 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17387] VGAM1245 gene, herein designated VGAM GENE, encodes a VGAM1245 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1245 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1245 precursor RNA is designated SEQ ID:31999, and is provided hereinbelow with reference to the sequence listing part.

[17388] VGAM1245 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17389] An enzyme complex designated DICER COMPLEX, dices the VGAM1245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1245 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1245 RNA is designated SEQ ID:32000, and is provided hereinbelow with reference to the sequence listing part.

[17390] VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17391] VGAM1245 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1245 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1245 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17392] The complementary binding of VGAM1245 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1245 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17393] It is appreciated that VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1245 host target genes. The mRNA of each one of this plurality of VGAM1245 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1245 RNA, herein designated VGAM RNA, and which when bound by VGAM1245 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1245 host target proteins.

[17394] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1245 gene, herein designated VGAM GENE, on one or more VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17395] It is yet further appreciated that a function of VGAM1245 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1245 include diagnosis, prevention and



treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1245 correlate with, and may be deduced from, the identity of the host target genes which VGAM1245 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17396] Nucleotide sequences of the VGAM1245 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1245 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1245 are further described hereinbelow with reference to Table 1.

[17397] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1245 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17398] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1246 (VGAM1246) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17399] VGAM1246 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1246 was detected is described hereinabove with reference to Figs. 2–8.

[17400] VGAM1246 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17401] VGAM1246 gene, herein designated VGAM GENE, encodes a VGAM1246 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1246 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1246 precursor RNA is designated SEQ ID:32097, and is provided hereinbelow with reference to the sequence listing part.

[17402] VGAM1246 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1246 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17403] An enzyme complex designated DICER COMPLEX, dices the VGAM1246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1246 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1246 RNA is designated SEQ ID:32098, and is provided hereinbelow with reference to the sequence listing part.

[17404] VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1246 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17405] VGAM1246 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1246 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17406] The complementary binding of VGAM1246 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1246 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17407] It is appreciated that VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1246 host target genes. The mRNA of each one of this plurality of VGAM1246 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1246 RNA, herein designated VGAM RNA, and which when bound by VGAM1246 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1246 host target proteins.

[17408] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1246 gene, herein designated VGAM GENE, on one or more VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17409] It is yet further appreciated that a function of VGAM1246 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific

functions, and accordingly utilities, of VGAM1246 correlate with, and may be deduced from, the identity of the host target genes which VGAM1246 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17410] Nucleotide sequences of the VGAM1246 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1246 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1246 are further described hereinbelow with reference to Table 1.

[17411] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1246 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17412] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1247 (VGAM1247) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[17413] VGAM1247 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1247 was detected is described hereinabove with reference to Figs. 2–8.

[17414] VGAM1247 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17415] VGAM1247 gene, herein designated VGAM GENE, encodes a VGAM1247 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1247 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1247 precursor RNA is designated SEQ ID:32112, and is provided hereinbelow with reference to the sequence listing part.

[17416] VGAM1247 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1247 folded precursor RNA, herein designated VGAM FOLDED PRECUR-



SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17417] An enzyme complex designated DICER COMPLEX, dices the VGAM1247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1247 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1247 RNA is designated SEQ ID:32113, and is provided hereinbelow with reference to the sequence listing part.

[17418] VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1247 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17419] VGAM1247 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1247 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1247 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17420] The complementary binding of VGAM1247 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1247 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17421] It is appreciated that VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1247 host target genes. The mRNA of each one of this plurality of VGAM1247 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1247 RNA, herein designated VGAM RNA, and which when bound by VGAM1247 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1247 host target proteins.

[17422] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1247 gene, herein designated VGAM GENE, on one or more VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17423] It is yet further appreciated that a function of VGAM1247 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1247 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1247

correlate with, and may be deduced from, the identity of the host target genes which VGAM1247 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17424] Nucleotide sequences of the VGAM1247 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1247 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1247 are further described hereinbelow with reference to Table 1.

[17425] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1247 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17426] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1248 (VGAM1248) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[17427] VGAM1248 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1248 was detected is described hereinabove with reference to Figs. 2–8.

[17428] VGAM1248 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17429] VGAM1248 gene, herein designated VGAM GENE, encodes a VGAM1248 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1248 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1248 precursor RNA is designated SEQ ID:32118, and is provided hereinbelow with reference to the sequence listing part.

[17430] VGAM1248 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17431] An enzyme complex designated DICER COMPLEX, dices the VGAM1248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1248 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1248 RNA is designated SEQ ID:32119, and is provided hereinbelow with reference to the sequence listing part.

[17432] VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17433] VGAM1248 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1248 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an



example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17434] The complementary binding of VGAM1248 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1248 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17435] It is appreciated that VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1248 host target genes. The mRNA of each one of this plurality of VGAM1248 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1248 RNA, herein designated VGAM RNA, and which when bound by VGAM1248 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1248 host target proteins.

[17436] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1248 gene, herein designated VGAM GENE, on one or more VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17437] It is yet further appreciated that a function of VGAM1248 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1248 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1248 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17438] Nucleotide sequences of the VGAM1248 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1248 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1248 are further described hereinbelow with reference to Table 1.

[17439] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1248 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17440] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1249 (VGAM1249) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17441] VGAM1249 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1249 was detected is described hereinabove with reference to Figs. 2–8.

[17442] VGAM1249 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Drosophila C virus. VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17443] VGAM1249 gene, herein designated VGAM GENE, encodes a VGAM1249 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1249 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1249 precursor RNA is designated SEQ ID:32123, and is provided hereinbelow with reference to the sequence listing part.

[17444] VGAM1249 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17445] An enzyme complex designated DICER COMPLEX, dices the VGAM1249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1249 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1249 RNA is designated SEQ ID:32124, and is provided hereinbelow with reference to the sequence listing part.

[17446] VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17447] VGAM1249 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1249 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17448] The complementary binding of VGAM1249 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1249 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17449] It is appreciated that VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1249 host target genes. The mRNA of each one of this plurality of VGAM1249 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1249 RNA, herein designated VGAM RNA, and which when bound by VGAM1249 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1249 host target proteins.

[17450] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1249 gene, herein designated VGAM GENE, on one or more VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17451] It is yet further appreciated that a function of VGAM1249 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of viral infection by Drosophila C virus. Specific functions, and accordingly utilities, of VGAM1249 correlate with, and may be deduced from, the identity of the host target genes which VGAM1249 binds and inhibits,



and the function of these host target genes, as elaborated hereinbelow.

[17452] Nucleotide sequences of the VGAM1249 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1249 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1249 are further described hereinbelow with reference to Table 1.

[17453] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1249 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17454] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1250 (VGAM1250) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17455] VGAM1250 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1250 was detected is described hereinabove with reference to Figs. 2–8.

[17456] VGAM1250 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Drosophila C virus.

VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17457] VGAM1250 gene, herein designated VGAM GENE, encodes a VGAM1250 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1250 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1250 precursor RNA is designated SEQ ID:32127, and is provided hereinbelow with reference to the sequence listing part.

[17458] VGAM1250 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17459] An enzyme complex designated DICER COMPLEX, dices the VGAM1250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1250 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1250 RNA is designated SEQ ID:32128, and is provided hereinbelow with reference to the sequence listing part.

[17460] VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17461] VGAM1250 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1250 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3'UTR and 5'UTR regions.

[17462] The complementary binding of VGAM1250 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1250 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17463] It is appreciated that VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1250 host target genes. The mRNA of each one of this plurality of VGAM1250 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1250 RNA, herein designated VGAM RNA, and which when bound by VGAM1250 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1250 host target proteins.

[17464] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1250 gene, herein designated VGAM GENE, on one or more VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17465] It is yet further appreciated that a function of VGAM1250 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of viral infection by Drosophila C virus. Specific functions, and accordingly utilities, of VGAM1250 correlate with, and may be deduced from, the identity of the host target genes which VGAM1250 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[17466] Nucleotide sequences of the VGAM1250 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1250 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1250 are further described hereinbelow with reference to Table 1.

[17467] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1250 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17468] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1251 (VGAM1251) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17469] VGAM1251 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1251 was detected is described hereinabove with reference to Figs. 2–8.

[17470] VGAM1251 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17471] VGAM1251 gene, herein designated VGAM GENE, encodes a VGAM1251 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1251 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1251 precursor RNA is designated SEQ ID:32137, and is provided hereinbelow with reference to the sequence listing part.

[17472] VGAM1251 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the



RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17473] An enzyme complex designated DICER COMPLEX, dices the VGAM1251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1251 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1251 RNA is designated SEQ ID:32138, and is provided hereinbelow with reference to the sequence listing part.

[17474] VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[17475] VGAM1251 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1251 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17476] The complementary binding of VGAM1251 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1251 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17477] It is appreciated that VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1251 host target genes. The mRNA of each one of this plurality of VGAM1251 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1251 RNA, herein designated VGAM RNA, and which when bound by VGAM1251 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1251 host target proteins.

[17478] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1251 gene, herein designated VGAM GENE, on one

or more VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17479] It is yet further appreciated that a function of VGAM1251 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1251 correlate with, and may be deduced from, the identity of the host target genes which VGAM1251 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17480] Nucleotide sequences of the VGAM1251 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1251 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1251 are further described hereinbelow with reference to Table 1.

[17481] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1251 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17482] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1252 (VGAM1252) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17483] VGAM1252 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1252 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[17484] VGAM1252 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 4. VGAM1252 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17485] VGAM1252 gene, herein designated VGAM GENE, encodes a VGAM1252 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1252 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1252 precursor RNA is designated SEQ ID:32156, and is provided hereinbelow with reference to the sequence listing part.

[17486] VGAM1252 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17487] An enzyme complex designated DICER COMPLEX, dices the VGAM1252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1252 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1252 RNA is designated SEQ ID:32157, and is provided hereinbelow with reference to the sequence listing part.

[17488] VGAM1252 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17489] VGAM1252 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1252 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17490] The complementary binding of VGAM1252 RNA, herein



designated VGAM RNA, to host target binding sites on VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1252 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17491] It is appreciated that VGAM1252 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1252 host target genes. The mRNA of each one of this plurality of VGAM1252 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1252 RNA, herein designated VGAM RNA, and which when bound by VGAM1252 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1252 host target proteins.

[17492] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1252 gene, herein designated VGAM GENE, on one or more VGAM1252 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17493] It is yet further appreciated that a function of VGAM1252 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1252 correlate with, and may be deduced from, the identity of the host target genes which VGAM1252 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17494] Nucleotide sequences of the VGAM1252 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1252 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1252 are further described hereinbelow with reference to Table 1.

[17495] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1252 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17496] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1253 (VGAM1253) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17497] VGAM1253 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1253 was detected is described hereinabove with reference to Figs. 2-8.

[17498] VGAM1253 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A.

VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17499] VGAM1253 gene, herein designated VGAM GENE, encodes a VGAM1253 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1253 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1253 precursor RNA is designated SEQ ID:32185, and is provided hereinbelow with reference to the sequence listing part.

[17500] VGAM1253 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[17501] An enzyme complex designated DICER COMPLEX, dices the VGAM1253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1253 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1253 RNA is designated SEQ ID:32186, and is provided hereinbelow with reference to the sequence listing part.

[17502] VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17503] VGAM1253 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1253 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1253 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17504] The complementary binding of VGAM1253 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1253 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17505] It is appreciated that VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1253 host target genes. The mRNA of each one of this plurality of VGAM1253 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1253 RNA, herein designated VGAM RNA, and which when bound by VGAM1253 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1253 host target proteins.

[17506] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1253 gene, herein designated VGAM GENE, on one or more VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17507] It is yet further appreciated that a function of VGAM1253 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1253 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM1253 correlate with, and may be deduced from, the identity of the host target genes which VGAM1253 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17508] Nucleotide sequences of the VGAM1253 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the



diced VGAM1253 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1253 are further described hereinbelow with reference to Table 1.

[17509] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1253 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17510] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1254 (VGAM1254) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17511] VGAM1254 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1254 was detected is described hereinabove with reference to Figs. 2-8.

[17512] VGAM1254 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Ovine adenovirus A. VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17513] VGAM1254 gene, herein designated VGAM GENE, encodes a VGAM1254 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1254 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1254 precursor RNA is designated SEQ ID:32211, and is provided hereinbelow with reference to the sequence listing part.

[17514] VGAM1254 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17515] An enzyme complex designated DICER COMPLEX, dices the VGAM1254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1254 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1254 RNA is designated SEQ ID:32212, and is provided hereinbelow with reference to the sequence listing part.

[17516] VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17517] VGAM1254 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1254 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17518] The complementary binding of VGAM1254 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1254 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1254 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17519] It is appreciated that VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1254 host target genes. The mRNA of each one of this plurality of VGAM1254 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1254 RNA, herein designated VGAM RNA, and which when bound by VGAM1254 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1254 host target proteins.

[17520] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1254 gene, herein designated VGAM GENE, on one or more VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17521] It is yet further appreciated that a function of VGAM1254 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of viral infection by Ovine adenovirus A. Specific functions, and accordingly utilities, of VGAM1254 correlate with, and may be deduced from, the identity of the host target genes which VGAM1254 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17522] Nucleotide sequences of the VGAM1254 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1254 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1254 are further described hereinbelow with reference to Table 1.

[17523] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1254 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17524] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1255 (VGAM1255) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17525] VGAM1255 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1255 was detected is described hereinabove with reference to Figs. 2-8.

[17526] VGAM1255 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ovine adenovirus A.

VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17527] VGAM1255 gene, herein designated VGAM GENE, encodes a VGAM1255 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1255 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1255 precursor RNA is designated SEQ ID:32224, and is provided hereinbelow with reference to the sequence listing part.

[17528] VGAM1255 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17529] An enzyme complex designated DICER COMPLEX, dices



the VGAM1255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1255 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1255 RNA is designated SEQ ID:32225, and is provided hereinbelow with reference to the sequence listing part.

[17530] VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17531] VGAM1255 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1255 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1255 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17532] The complementary binding of VGAM1255 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1255 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17533] It is appreciated that VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1255 host target genes. The mRNA of each one of this plurality of VGAM1255 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1255 RNA, herein designated VGAM RNA, and which when bound by VGAM1255 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1255 host target proteins.

[17534] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1255 gene, herein designated VGAM GENE, on one or more VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17535] It is yet further appreciated that a function of VGAM1255 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of viral infection by Ovine adenovirus A. Specific functions, and accordingly utilities, of VGAM1255 correlate with, and may be deduced from, the identity of the host target genes which VGAM1255 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17536] Nucleotide sequences of the VGAM1255 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1255 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1255 are further described hereinbelow with reference to Table 1.

[17537] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1255 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17538] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1256 (VGAM1256) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17539] VGAM1256 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1256 was detected is described hereinabove with reference to Figs. 2-8.

[17540] VGAM1256 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus.

VGAM1256 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[17541] VGAM1256 gene, herein designated VGAM GENE, encodes a VGAM1256 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1256 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1256 precursor RNA is designated SEQ ID:32245, and is provided hereinbelow with reference to the sequence listing part.

[17542] VGAM1256 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1256 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17543] An enzyme complex designated DICER COMPLEX, dices the VGAM1256 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1256 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1256 RNA is designated SEQ ID:32246, and is provided hereinbelow with reference to the sequence listing part.

[17544] VGAM1256 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17545] VGAM1256 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1256 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17546] The complementary binding of VGAM1256 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1256



host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1256 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17547] It is appreciated that VGAM1256 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1256 host target genes. The mRNA of each one of this plurality of VGAM1256 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1256 RNA, herein designated VGAM RNA, and which when bound by VGAM1256 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1256 host target proteins.

[17548] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1256 gene, herein designated VGAM GENE, on one or more VGAM1256 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17549] It is yet further appreciated that a function of VGAM1256 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM1256 correlate with, and may be deduced from, the identity of the host target genes which VGAM1256 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17550] Nucleotide sequences of the VGAM1256 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1256 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1256 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1256 are further described hereinbelow with reference to Table 1.

[17551] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1256 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17552] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1257 (VGAM1257) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17553] VGAM1257 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1257 was detected is described hereinabove with reference to Figs. 2-8.

[17554] VGAM1257 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[17555] VGAM1257 gene, herein designated VGAM GENE, encodes a VGAM1257 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1257 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1257 precursor RNA is designated SEQ ID:32255, and is provided hereinbelow with reference to the sequence listing part.

[17556] VGAM1257 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17557] An enzyme complex designated DICER COMPLEX, dices the VGAM1257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1257 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1257 RNA is designated SEQ ID:32256, and is provided hereinbelow with reference to the sequence listing part.

[17558] VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17559] VGAM1257 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1257 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17560] The complementary binding of VGAM1257 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1257 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1257 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17561] It is appreciated that VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1257 host target genes. The mRNA of each one of this plurality of VGAM1257 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1257 RNA, herein designated VGAM RNA, and which when bound by VGAM1257 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1257 host target proteins.

[17562] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1257 gene, herein designated VGAM GENE, on one or more VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17563] It is yet further appreciated that a function of VGAM1257 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1257 correlate with, and may be deduced from, the identity of the host target genes which VGAM1257 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17564] Nucleotide sequences of the VGAM1257 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1257 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1257 are further



described hereinbelow with reference to Table 1.

[17565] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1257 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17566] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1258 (VGAM1258) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17567] VGAM1258 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1258 was detected is described hereinabove with reference to Figs. 2-8.

[17568] VGAM1258 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus. VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17569] VGAM1258 gene, herein designated VGAM GENE, encodes a VGAM1258 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1258 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1258 precursor RNA is designated SEQ ID:32303, and is provided hereinbelow with reference to the sequence listing part.

[17570] VGAM1258 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17571] An enzyme complex designated DICER COMPLEX, dices the VGAM1258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1258 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1258 RNA is designated SEQ ID:32304, and is provided hereinbelow with reference to the sequence listing part.

[17572] VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17573] VGAM1258 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1258 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1258 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17574] The complementary binding of VGAM1258 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1258 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17575] It is appreciated that VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1258 host target genes. The mRNA of each one of this plurality of VGAM1258 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1258 RNA, herein designated VGAM RNA, and which when bound by VGAM1258 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1258 host target proteins.

[17576] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1258 gene, herein designated VGAM GENE, on one or more VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17577] It is yet further appreciated that a function of VGAM1258 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM1258 correlate with, and may be deduced from, the identity of the host target genes which VGAM1258 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17578] Nucleotide sequences of the VGAM1258 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1258 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1258 are further described hereinbelow with reference to Table 1.

[17579] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1258 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17580] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1259 (VGAM1259) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17581] VGAM1259 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1259 was detected is described hereinabove with reference to Figs. 2-8.

[17582] VGAM1259 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17583] VGAM1259 gene, herein designated VGAM GENE, encodes

a VGAM1259 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1259 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1259 precursor RNA is designated SEQ ID:32311, and is provided hereinbelow with reference to the sequence listing part.

[17584] VGAM1259 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17585] An enzyme complex designated DICER COMPLEX, dices the VGAM1259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1259 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a



hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1259 RNA is designated SEQ ID:32312, and is provided hereinbelow with reference to the sequence listing part.

[17586] VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17587] VGAM1259 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1259 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17588] The complementary binding of VGAM1259 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1259 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[17589] It is appreciated that VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1259 host target genes. The mRNA of each one of this plurality of VGAM1259 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1259 RNA, herein designated VGAM RNA, and which when bound by VGAM1259 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1259 host target proteins.

[17590] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1259 gene, herein designated VGAM GENE, on one or more VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17591] It is yet further appreciated that a function of VGAM1259 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1259 correlate with, and may be deduced from, the identity of the host target genes which VGAM1259 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17592] Nucleotide sequences of the VGAM1259 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1259 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1259 are further described hereinbelow with reference to Table 1.

[17593] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1259 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17594] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1260 (VGAM1260) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17595] VGAM1260 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1260 was detected is described hereinabove with reference to Figs. 2-8.

[17596] VGAM1260 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6. VGAM1260 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17597] VGAM1260 gene, herein designated VGAM GENE, encodes a VGAM1260 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1260 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1260 precursor RNA is designated SEQ ID:32321, and is provided hereinbelow with reference to the sequence listing part.

[17598] VGAM1260 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17599] An enzyme complex designated DICER COMPLEX, dices the VGAM1260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1260 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1260 RNA is designated SEQ ID:32322, and is provided hereinbelow with reference to the sequence listing part.

[17600] VGAM1260 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17601] VGAM1260 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1260 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17602] The complementary binding of VGAM1260 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1260 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.



[17603] It is appreciated that VGAM1260 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1260 host target genes. The mRNA of each one of this plurality of VGAM1260 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1260 RNA, herein designated VGAM RNA, and which when bound by VGAM1260 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1260 host target proteins.

[17604] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1260 gene, herein designated VGAM GENE, on one or more VGAM1260 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17605] It is yet further appreciated that a function of VGAM1260 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1260 correlate with, and may be deduced from, the identity of the host target genes which VGAM1260 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17606] Nucleotide sequences of the VGAM1260 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1260 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1260 are further described hereinbelow with reference to Table 1.

[17607] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1260 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17608] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1261 (VGAM1261) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17609] VGAM1261 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1261 was detected is described hereinabove with reference to Figs. 2-8.

[17610] VGAM1261 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1261 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17611] VGAM1261 gene, herein designated VGAM GENE, encodes a VGAM1261 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1261 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1261 precursor RNA is designated SEQ ID:32333, and is provided hereinbelow with reference to the sequence listing part.

[17612] VGAM1261 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17613] An enzyme complex designated DICER COMPLEX, dices the VGAM1261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1261 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1261 RNA is designated SEQ ID:32334, and is provided hereinbelow with reference to the sequence listing part.

[17614] VGAM1261 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17615] VGAM1261 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1261 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1261 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17616] The complementary binding of VGAM1261 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1261 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17617] It is appreciated that VGAM1261 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1261 host target genes. The mRNA of each one of this plurality of VGAM1261 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1261 RNA, herein designated VGAM RNA, and which when bound by VGAM1261 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1261 host target proteins.

[17618] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1261 gene, herein designated VGAM GENE, on one or more VGAM1261 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17619] It is yet further appreciated that a function of VGAM1261 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1261 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1261 correlate with, and may be deduced from, the identity of the host target genes which VGAM1261 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17620] Nucleotide sequences of the VGAM1261 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1261 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1261 are further described hereinbelow with reference to Table 1.

[17621] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the



complementarity of each of these host target binding sites to VGAM1261 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17622] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1262 (VGAM1262) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17623] VGAM1262 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1262 was detected is described hereinabove with reference to Figs. 2–8.

[17624] VGAM1262 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17625] VGAM1262 gene, herein designated VGAM GENE, encodes a VGAM1262 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1262 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1262 precursor RNA is designated SEQ ID:32354, and is provided hereinbelow with reference to the sequence listing part.

[17626] VGAM1262 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17627] An enzyme complex designated DICER COMPLEX, dices the VGAM1262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1262 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1262 RNA is designated SEQ ID:32355, and is provided hereinbelow with reference to the sequence listing part.

[17628] VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17629] VGAM1262 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1262 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1262 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17630] The complementary binding of VGAM1262 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1262 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17631] It is appreciated that VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1262 host target genes. The mRNA of each one of this plurality of VGAM1262 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1262 RNA, herein designated VGAM RNA, and which when bound by VGAM1262 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1262 host target proteins.

[17632] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1262 gene, herein designated VGAM GENE, on one or more VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [17633] It is yet further appreciated that a function of VGAM1262 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1262 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1262 correlate with, and may be deduced from, the identity of the host target genes which VGAM1262 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [17634] Nucleotide sequences of the VGAM1262 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1262 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1262 are further described hereinbelow with reference to Table 1.
- [17635] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1262 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17636] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1263 (VGAM1263) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17637] VGAM1263 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1263 was detected is described hereinabove with reference to Figs. 2-8.

[17638] VGAM1263 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17639] VGAM1263 gene, herein designated VGAM GENE, encodes a VGAM1263 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1263 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1263 precursor RNA is designated SEQ ID:32368, and is provided hereinbelow with reference to the sequence listing part.

[17640] VGAM1263 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17641] An enzyme complex designated DICER COMPLEX, dices the VGAM1263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1263 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-



quence of VGAM1263 RNA is designated SEQ ID:32369, and is provided hereinbelow with reference to the sequence listing part.

[17642] VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17643] VGAM1263 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1263 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17644] The complementary binding of VGAM1263 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1263 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17645] It is appreciated that VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1263 host target genes. The mRNA of

each one of this plurality of VGAM1263 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1263 RNA, herein designated VGAM RNA, and which when bound by VGAM1263 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1263 host target proteins.

[17646] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1263 gene, herein designated VGAM GENE, on one or more VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[17647] It is yet further appreciated that a function of VGAM1263 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1263 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1263 correlate with, and may be deduced from, the identity of the host target genes which VGAM1263 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17648] Nucleotide sequences of the VGAM1263 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1263 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1263 are further described hereinbelow with reference to Table 1.

[17649] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1263 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[17650] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1264 (VGAM1264) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17651] VGAM1264 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1264 was detected is described hereinabove with reference to Figs. 2–8.

[17652] VGAM1264 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17653] VGAM1264 gene, herein designated VGAM GENE, encodes a VGAM1264 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1264 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1264 precursor RNA is designated SEQ ID:32376, and is provided hereinbelow with reference to the sequence listing part.

[17654] VGAM1264 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17655] An enzyme complex designated DICER COMPLEX, dices the VGAM1264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1264 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1264 RNA is designated SEQ ID:32377,

and is provided hereinbelow with reference to the sequence listing part.

[17656] VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17657] VGAM1264 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1264 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17658] The complementary binding of VGAM1264 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1264 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17659] It is appreciated that VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1264 host target genes. The mRNA of each one of this plurality of VGAM1264 host target genes



comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1264 RNA, herein designated VGAM RNA, and which when bound by VGAM1264 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1264 host target proteins.

[17660] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1264 gene, herein designated VGAM GENE, on one or more VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17661] It is yet further appreciated that a function of VGAM1264 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1264 correlate with, and may be deduced from, the identity of the host target genes which VGAM1264 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17662] Nucleotide sequences of the VGAM1264 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1264 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1264 are further described hereinbelow with reference to Table 1.

[17663] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1264 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17664] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1265 (VGAM1265) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17665] VGAM1265 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1265 was detected is described hereinabove with reference to Figs. 2–8.

[17666] VGAM1265 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17667] VGAM1265 gene, herein designated VGAM GENE, encodes a VGAM1265 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1265 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1265 precu-

sor RNA is designated SEQ ID:32401, and is provided hereinbelow with reference to the sequence listing part.

[17668] VGAM1265 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17669] An enzyme complex designated DICER COMPLEX, dices the VGAM1265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1265 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1265 RNA is designated SEQ ID:32402, and is provided hereinbelow with reference to the se-

quence listing part.

[17670] VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17671] VGAM1265 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1265 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17672] The complementary binding of VGAM1265 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1265 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17673] It is appreciated that VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1265 host target genes. The mRNA of each one of this plurality of VGAM1265 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1265 RNA, herein designated VGAM RNA, and which when bound by VGAM1265 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1265 host target proteins.

[17674] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1265 gene, herein designated VGAM GENE, on one or more VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17675] It is yet further appreciated that a function of VGAM1265

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM1265 correlate with, and may be deduced from, the identity of the host target genes which VGAM1265 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17676] Nucleotide sequences of the VGAM1265 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1265 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1265 are further described hereinbelow with reference to Table 1.

[17677] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1265 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17678] Fig. 1 further provides a conceptual description of another



novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1266 (VGAM1266) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17679] VGAM1266 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1266 was detected is described hereinabove with reference to Figs. 2–8.

[17680] VGAM1266 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17681] VGAM1266 gene, herein designated VGAM GENE, encodes a VGAM1266 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1266 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1266 precursor RNA is designated SEQ ID:32412, and is provided

hereinbelow with reference to the sequence listing part.

[17682] VGAM1266 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17683] An enzyme complex designated DICER COMPLEX, dices the VGAM1266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1266 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1266 RNA is designated SEQ ID:32413, and is provided hereinbelow with reference to the sequence listing part.

[17684] VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17685] VGAM1266 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1266 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1266 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17686] The complementary binding of VGAM1266 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1266 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17687] It is appreciated that VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1266 host target genes. The mRNA of each one of this plurality of VGAM1266 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1266 RNA, herein designated VGAM RNA, and which when bound by VGAM1266 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1266 host target proteins.

[17688] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1266 gene, herein designated VGAM GENE, on one or more VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17689] It is yet further appreciated that a function of VGAM1266 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1266 correlate with, and may be deduced from, the identity of the host target genes which VGAM1266 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17690] Nucleotide sequences of the VGAM1266 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1266 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1266 are further described hereinbelow with reference to Table 1.

[17691] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1266 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17692] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1267 (VGAM1267) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17693] VGAM1267 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1267 was detected is described hereinabove with reference to Figs. 2–8.

[17694] VGAM1267 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola virus. VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17695] VGAM1267 gene, herein designated VGAM GENE, encodes a VGAM1267 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1267 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1267 precursor RNA is designated SEQ ID:32430, and is provided hereinbelow with reference to the sequence listing part.

[17696] VGAM1267 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17697] An enzyme complex designated DICER COMPLEX, dices the VGAM1267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1267 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1267 RNA is designated SEQ ID:32431, and is provided hereinbelow with reference to the sequence listing part.

[17698] VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17699] VGAM1267 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1267 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1267 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1267 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17700] The complementary binding of VGAM1267 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1267 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17701] It is appreciated that VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1267 host target genes. The mRNA of each one of this plurality of VGAM1267 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1267 RNA, herein designated VGAM RNA, and which when bound by VGAM1267 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1267 host target proteins.

[17702] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1267 gene, herein designated VGAM GENE, on one or more VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17703] It is yet further appreciated that a function of VGAM1267 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1267 include diagnosis, prevention and

treatment of viral infection by Variola virus. Specific functions, and accordingly utilities, of VGAM1267 correlate with, and may be deduced from, the identity of the host target genes which VGAM1267 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17704] Nucleotide sequences of the VGAM1267 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1267 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1267 are further described hereinbelow with reference to Table 1.

[17705] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1267 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17706] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1268 (VGAM1268) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17707] VGAM1268 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1268 was detected is described hereinabove with reference to Figs. 2–8.

[17708] VGAM1268 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17709] VGAM1268 gene, herein designated VGAM GENE, encodes a VGAM1268 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1268 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1268 precursor RNA is designated SEQ ID:32436, and is provided hereinbelow with reference to the sequence listing part.

[17710] VGAM1268 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1268 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17711] An enzyme complex designated DICER COMPLEX, dices the VGAM1268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1268 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1268 RNA is designated SEQ ID:32437, and is provided hereinbelow with reference to the sequence listing part.

[17712] VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1268 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17713] VGAM1268 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1268 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1268 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17714] The complementary binding of VGAM1268 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1268 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17715] It is appreciated that VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1268 host target genes. The mRNA of each one of this plurality of VGAM1268 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1268 RNA, herein designated VGAM RNA, and which when bound by VGAM1268 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM1268 host target proteins.

[17716] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1268 gene, herein designated VGAM GENE, on one or more VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17717] It is yet further appreciated that a function of VGAM1268 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1268 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Spe-

cific functions, and accordingly utilities, of VGAM1268 correlate with, and may be deduced from, the identity of the host target genes which VGAM1268 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17718] Nucleotide sequences of the VGAM1268 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1268 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1268 are further described hereinbelow with reference to Table 1.

[17719] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1268 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17720] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1269 (VGAM1269) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[17721] VGAM1269 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1269 was detected is described hereinabove with reference to Figs. 2–8.

[17722] VGAM1269 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 1. VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17723] VGAM1269 gene, herein designated VGAM GENE, encodes a VGAM1269 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1269 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1269 precursor RNA is designated SEQ ID:32665, and is provided hereinbelow with reference to the sequence listing part.

[17724] VGAM1269 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1269 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17725] An enzyme complex designated DICER COMPLEX, dices the VGAM1269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1269 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1269 RNA is designated SEQ ID:32666, and is provided hereinbelow with reference to the sequence listing part.

[17726] VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1269 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17727] VGAM1269 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1269 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1269 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17728] The complementary binding of VGAM1269 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1269 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17729] It is appreciated that VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1269 host target genes. The mRNA of each one of this plurality of VGAM1269 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1269 RNA, herein designated VGAM RNA, and which when bound by VGAM1269 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1269 host target proteins.

[17730] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1269 gene, herein designated VGAM GENE, on one or more VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17731] It is yet further appreciated that a function of VGAM1269 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1269 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1269

correlate with, and may be deduced from, the identity of the host target genes which VGAM1269 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17732] Nucleotide sequences of the VGAM1269 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1269 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1269 are further described hereinbelow with reference to Table 1.

[17733] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1269 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17734] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1270 (VGAM1270) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[17735] VGAM1270 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1270 was detected is described hereinabove with reference to Figs. 2–8.

[17736] VGAM1270 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17737] VGAM1270 gene, herein designated VGAM GENE, encodes a VGAM1270 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1270 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1270 precursor RNA is designated SEQ ID:32824, and is provided hereinbelow with reference to the sequence listing part.

[17738] VGAM1270 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17739] An enzyme complex designated DICER COMPLEX, dices the VGAM1270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1270 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1270 RNA is designated SEQ ID:32825, and is provided hereinbelow with reference to the sequence listing part.

[17740] VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17741] VGAM1270 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1270 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1270 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17742] The complementary binding of VGAM1270 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1270 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17743] It is appreciated that VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1270 host target genes. The mRNA of each one of this plurality of VGAM1270 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1270 RNA, herein designated VGAM RNA, and which when bound by VGAM1270 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1270 host target proteins.

[17744] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1270 gene, herein designated VGAM GENE, on one or more VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17745] It is yet further appreciated that a function of VGAM1270 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1270 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1270 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1270 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17746] Nucleotide sequences of the VGAM1270 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1270 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1270 are further described hereinbelow with reference to Table 1.

[17747] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1270 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17748] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1271 (VGAM1271) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17749] VGAM1271 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1271 was detected is described hereinabove with reference to Figs. 2–8.

[17750] VGAM1271 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17751] VGAM1271 gene, herein designated VGAM GENE, encodes a VGAM1271 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1271 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1271 precursor RNA is designated SEQ ID:32835, and is provided hereinbelow with reference to the sequence listing part.

[17752] VGAM1271 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17753] An enzyme complex designated DICER COMPLEX, dices the VGAM1271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1271 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1271 RNA is designated SEQ ID:32836, and is provided hereinbelow with reference to the sequence listing part.

[17754] VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding



gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17755] VGAM1271 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1271 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17756] The complementary binding of VGAM1271 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1271 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17757] It is appreciated that VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1271 host target genes. The mRNA of each one of this plurality of VGAM1271 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1271 RNA, herein designated VGAM RNA, and which when bound by VGAM1271 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1271 host target proteins.

[17758] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1271 gene, herein designated VGAM GENE, on one or more VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17759] It is yet further appreciated that a function of VGAM1271 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM1271 correlate with, and may be deduced from, the identity of the host target genes which

VGAM1271 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17760] Nucleotide sequences of the VGAM1271 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1271 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1271 are further described hereinbelow with reference to Table 1.

[17761] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1271 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17762] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1272 (VGAM1272) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17763] VGAM1272 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1272 was detected is described hereinabove with reference to Figs. 2–8.

[17764] VGAM1272 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17765] VGAM1272 gene, herein designated VGAM GENE, encodes a VGAM1272 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1272 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1272 precursor RNA is designated SEQ ID:32839, and is provided hereinbelow with reference to the sequence listing part.

[17766] VGAM1272 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17767] An enzyme complex designated DICER COMPLEX, dices the VGAM1272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1272 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1272 RNA is designated SEQ ID:32840, and is provided hereinbelow with reference to the sequence listing part.

[17768] VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17769] VGAM1272 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1272 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[17770] The complementary binding of VGAM1272 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1272 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17771] It is appreciated that VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1272 host target genes. The mRNA of each one of this plurality of VGAM1272 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1272 RNA, herein designated VGAM RNA, and which when bound by VGAM1272 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1272 host target proteins.

[17772] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM1272 gene, herein designated VGAM GENE, on one or more VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17773] It is yet further appreciated that a function of VGAM1272 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1272 correlate with, and may be deduced from, the identity of the host target genes which VGAM1272 binds and inhibits, and the function of these host target

genes, as elaborated hereinbelow.

[17774] Nucleotide sequences of the VGAM1272 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1272 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1272 are further described hereinbelow with reference to Table 1.

[17775] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1272 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17776] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1273 (VGAM1273) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17777] VGAM1273 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1273 was detected is described hereinabove with reference to Figs. 2–8.

[17778] VGAM1273 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 17. VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17779] VGAM1273 gene, herein designated VGAM GENE, encodes a VGAM1273 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1273 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1273 precursor RNA is designated SEQ ID:32850, and is provided hereinbelow with reference to the sequence listing part.

[17780] VGAM1273 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17781] An enzyme complex designated DICER COMPLEX, dices the VGAM1273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1273 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1273 RNA is designated SEQ ID:32851, and is provided hereinbelow with reference to the sequence listing part.

[17782] VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[17783] VGAM1273 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1273 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17784] The complementary binding of VGAM1273 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1273 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17785] It is appreciated that VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1273 host target genes. The mRNA of each one of this plurality of VGAM1273 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1273 RNA, herein designated VGAM RNA, and which when bound by VGAM1273 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1273 host target proteins.

[17786] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1273 gene, herein designated VGAM GENE, on one

or more VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17787] It is yet further appreciated that a function of VGAM1273 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 17. Specific functions, and accordingly utilities, of VGAM1273 correlate with, and may be deduced from, the identity of the host target genes which VGAM1273 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17788] Nucleotide sequences of the VGAM1273 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1273 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1273 are further described hereinbelow with reference to Table 1.

[17789] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1273 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17790] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1274 (VGAM1274) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17791] VGAM1274 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1274 was detected is de-



scribed hereinabove with reference to Figs. 2–8.

[17792] VGAM1274 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1274 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17793] VGAM1274 gene, herein designated VGAM GENE, encodes a VGAM1274 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1274 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1274 precursor RNA is designated SEQ ID:32860, and is provided hereinbelow with reference to the sequence listing part.

[17794] VGAM1274 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17795] An enzyme complex designated DICER COMPLEX, dices the VGAM1274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1274 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1274 RNA is designated SEQ ID:32861, and is provided hereinbelow with reference to the sequence listing part.

[17796] VGAM1274 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17797] VGAM1274 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1274 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1274 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17798] The complementary binding of VGAM1274 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1274 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17799] It is appreciated that VGAM1274 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1274 host target genes. The mRNA of each one of this plurality of VGAM1274 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1274 RNA, herein designated VGAM RNA, and which when bound by VGAM1274 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1274 host target proteins.

[17800] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1274 gene, herein designated VGAM GENE, on one or more VGAM1274 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17801] It is yet further appreciated that a function of VGAM1274 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1274 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1274 correlate with, and may be deduced from, the identity of the host target genes which VGAM1274 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17802] Nucleotide sequences of the VGAM1274 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1274 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1274 are further described hereinbelow with reference to Table 1.

[17803] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1274 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17804] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1275 (VGAM1275) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17805] VGAM1275 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1275 was detected is described hereinabove with reference to Figs. 2-8.

[17806] VGAM1275 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17807] VGAM1275 gene, herein designated VGAM GENE, encodes a VGAM1275 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1275 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1275 precursor RNA is designated SEQ ID:32865, and is provided hereinbelow with reference to the sequence listing part.

[17808] VGAM1275 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[17809] An enzyme complex designated DICER COMPLEX, dices the VGAM1275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1275 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1275 RNA is designated SEQ ID:32866, and is provided hereinbelow with reference to the sequence listing part.

[17810] VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17811] VGAM1275 RNA, herein designated VGAM RNA, binds



complementarily to one or more host target binding sites located in untranslated regions of VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1275 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1275 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17812] The complementary binding of VGAM1275 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1275 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17813] It is appreciated that VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1275 host target genes. The mRNA of each one of this plurality of VGAM1275 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1275 RNA, herein designated VGAM RNA, and which when bound by VGAM1275 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1275 host target proteins.

[17814] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1275 gene, herein designated VGAM GENE, on one or more VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17815] It is yet further appreciated that a function of VGAM1275 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1275 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1275 correlate with, and may be deduced from, the identity of the host target genes which VGAM1275 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17816] Nucleotide sequences of the VGAM1275 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1275 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1275 are further described hereinbelow with reference to Table 1.

[17817] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1275 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17818] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1276 (VGAM1276) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17819] VGAM1276 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1276 was detected is described hereinabove with reference to Figs. 2-8.

[17820] VGAM1276 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Melanoplus sanguinipes* entomopoxvirus. VGAM1276 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17821] VGAM1276 gene, herein designated VGAM GENE, encodes a VGAM1276 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1276 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1276 precursor RNA is designated SEQ ID:32875, and is provided hereinbelow with reference to the sequence listing part.

[17822] VGAM1276 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17823] An enzyme complex designated DICER COMPLEX, dices the VGAM1276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1276 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1276 RNA is designated SEQ ID:32876, and is provided hereinbelow with reference to the sequence listing part.

[17824] VGAM1276 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17825] VGAM1276 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1276 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17826] The complementary binding of VGAM1276 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1276 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1276 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17827] It is appreciated that VGAM1276 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1276 host target genes. The mRNA of each one of this plurality of VGAM1276 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1276 RNA, herein designated VGAM RNA, and which when bound by VGAM1276 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1276 host target proteins.

[17828] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1276 gene, herein designated VGAM GENE, on one or more VGAM1276 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17829] It is yet further appreciated that a function of VGAM1276 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1276 correlate with, and may be deduced from, the identity of the host target genes which VGAM1276 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17830] Nucleotide sequences of the VGAM1276 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1276 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1276 are further described hereinbelow with reference to Table 1.

[17831] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1276 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17832] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1277 (VGAM1277) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17833] VGAM1277 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1277 was detected is described hereinabove with reference to Figs. 2-8.

[17834] VGAM1277 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A.

VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17835] VGAM1277 gene, herein designated VGAM GENE, encodes a VGAM1277 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1277 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1277 precursor RNA is designated SEQ ID:32880, and is provided hereinbelow with reference to the sequence listing part.

[17836] VGAM1277 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17837] An enzyme complex designated DICER COMPLEX, dices

the VGAM1277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1277 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1277 RNA is designated SEQ ID:32881, and is provided hereinbelow with reference to the sequence listing part.

[17838] VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17839] VGAM1277 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1277 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1277 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17840] The complementary binding of VGAM1277 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1277 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17841] It is appreciated that VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1277 host target genes. The mRNA of each one of this plurality of VGAM1277 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1277 RNA, herein designated VGAM RNA, and which when bound by VGAM1277 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1277 host target proteins.

[17842] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1277 gene, herein designated VGAM GENE, on one or more VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17843] It is yet further appreciated that a function of VGAM1277 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM1277 correlate with, and may be deduced from, the identity of the host target genes which VGAM1277 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17844] Nucleotide sequences of the VGAM1277 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1277 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1277 are further described hereinbelow with reference to Table 1.

[17845] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1277 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17846] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1278 (VGAM1278) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17847] VGAM1278 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1278 was detected is described hereinabove with reference to Figs. 2-8.

[17848] VGAM1278 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 7. VGAM1278 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[17849] VGAM1278 gene, herein designated VGAM GENE, encodes a VGAM1278 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1278 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1278 precursor RNA is designated SEQ ID:32886, and is provided hereinbelow with reference to the sequence listing part.

[17850] VGAM1278 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17851] An enzyme complex designated DICER COMPLEX, dices the VGAM1278 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1278 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1278 RNA is designated SEQ ID:32887, and is provided hereinbelow with reference to the sequence listing part.

[17852] VGAM1278 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17853] VGAM1278 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1278 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1278 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17854] The complementary binding of VGAM1278 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1278

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1278 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17855] It is appreciated that VGAM1278 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1278 host target genes. The mRNA of each one of this plurality of VGAM1278 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1278 RNA, herein designated VGAM RNA, and which when bound by VGAM1278 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1278 host target proteins.

[17856] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1278 gene, herein designated VGAM GENE, on one or more VGAM1278 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17857] It is yet further appreciated that a function of VGAM1278 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1278 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1278 correlate with, and may be deduced from, the identity of the host target genes which VGAM1278 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17858] Nucleotide sequences of the VGAM1278 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1278 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1278 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1278 are further described hereinbelow with reference to Table 1.

[17859] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1278 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17860] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1279 (VGAM1279) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17861] VGAM1279 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1279 was detected is described hereinabove with reference to Figs. 2-8.

[17862] VGAM1279 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A. VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[17863] VGAM1279 gene, herein designated VGAM GENE, encodes a VGAM1279 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1279 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1279 precursor RNA is designated SEQ ID:32902, and is provided hereinbelow with reference to the sequence listing part.

[17864] VGAM1279 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17865] An enzyme complex designated DICER COMPLEX, dices the VGAM1279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1279 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1279 RNA is designated SEQ ID:32903, and is provided hereinbelow with reference to the sequence listing part.

[17866] VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17867] VGAM1279 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1279 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17868] The complementary binding of VGAM1279 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1279 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1279 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17869] It is appreciated that VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1279 host target genes. The mRNA of each one of this plurality of VGAM1279 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1279 RNA, herein designated VGAM RNA, and which when bound by VGAM1279 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1279 host target proteins.

[17870] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1279 gene, herein designated VGAM GENE, on one or more VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17871] It is yet further appreciated that a function of VGAM1279 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM1279 correlate with, and may be deduced from, the identity of the host target genes which VGAM1279 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17872] Nucleotide sequences of the VGAM1279 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1279 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1279 are further

described hereinbelow with reference to Table 1.

[17873] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1279 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17874] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1280 (VGAM1280) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17875] VGAM1280 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1280 was detected is described hereinabove with reference to Figs. 2-8.

[17876] VGAM1280 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl adenovirus A. VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17877] VGAM1280 gene, herein designated VGAM GENE, encodes a VGAM1280 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1280 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1280 precursor RNA is designated SEQ ID:32915, and is provided hereinbelow with reference to the sequence listing part.

[17878] VGAM1280 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17879] An enzyme complex designated DICER COMPLEX, dices the VGAM1280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1280 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1280 RNA is designated SEQ ID:32916, and is provided hereinbelow with reference to the sequence listing part.

[17880] VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17881] VGAM1280 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1280 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1280 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17882] The complementary binding of VGAM1280 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1280 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17883] It is appreciated that VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1280 host target genes. The mRNA of each one of this plurality of VGAM1280 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1280 RNA, herein designated VGAM RNA, and which when bound by VGAM1280 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1280 host target proteins.

[17884] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1280 gene, herein designated VGAM GENE, on one or more VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17885] It is yet further appreciated that a function of VGAM1280 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of viral infection by Fowl adenovirus A. Specific functions, and accordingly utilities, of VGAM1280 correlate with, and may be deduced from, the identity of the host target genes which VGAM1280 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17886] Nucleotide sequences of the VGAM1280 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1280 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1280 are further described hereinbelow with reference to Table 1.

[17887] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1280 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17888] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1281 (VGAM1281) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17889] VGAM1281 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1281 was detected is described hereinabove with reference to Figs. 2-8.

[17890] VGAM1281 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 3. VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17891] VGAM1281 gene, herein designated VGAM GENE, encodes

a VGAM1281 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1281 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1281 precursor RNA is designated SEQ ID:32958, and is provided hereinbelow with reference to the sequence listing part.

[17892] VGAM1281 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17893] An enzyme complex designated DICER COMPLEX, dices the VGAM1281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1281 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1281 RNA is designated SEQ ID:32959, and is provided hereinbelow with reference to the sequence listing part.

[17894] VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17895] VGAM1281 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1281 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17896] The complementary binding of VGAM1281 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1281 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[17897] It is appreciated that VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1281 host target genes. The mRNA of each one of this plurality of VGAM1281 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1281 RNA, herein designated VGAM RNA, and which when bound by VGAM1281 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1281 host target proteins.

[17898] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1281 gene, herein designated VGAM GENE, on one or more VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17899] It is yet further appreciated that a function of VGAM1281 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1281 correlate with, and may be deduced from, the identity of the host target genes which VGAM1281 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17900] Nucleotide sequences of the VGAM1281 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1281 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1281 are further described hereinbelow with reference to Table 1.

[17901] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1281 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17902] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1282 (VGAM1282) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17903] VGAM1282 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1282 was detected is described hereinabove with reference to Figs. 2-8.

[17904] VGAM1282 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Blackcurrant reversion virus. VGAM1282 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17905] VGAM1282 gene, herein designated VGAM GENE, encodes a VGAM1282 precursor RNA, herein designated VGAM



PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1282 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1282 precursor RNA is designated SEQ ID:33012, and is provided hereinbelow with reference to the sequence listing part.

[17906] VGAM1282 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17907] An enzyme complex designated DICER COMPLEX, dices the VGAM1282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1282 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1282 RNA is designated SEQ ID:33013, and is provided hereinbelow with reference to the sequence listing part.

[17908] VGAM1282 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17909] VGAM1282 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1282 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1282 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17910] The complementary binding of VGAM1282 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1282 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17911] It is appreciated that VGAM1282 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1282 host target genes. The mRNA of each one of this plurality of VGAM1282 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1282 RNA, herein designated VGAM RNA, and which when bound by VGAM1282 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1282 host target proteins.

[17912] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1282 gene, herein designated VGAM GENE, on one or more VGAM1282 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17913] It is yet further appreciated that a function of VGAM1282 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1282 include diagnosis, prevention and treatment of viral infection by Blackcurrant reversion virus. Specific functions, and accordingly utilities, of VGAM1282 correlate with, and may be deduced from, the identity of the host target genes which VGAM1282 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17914] Nucleotide sequences of the VGAM1282 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1282 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1282 are further described hereinbelow with reference to Table 1.

[17915] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1282 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17916] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1283 (VGAM1283) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17917] VGAM1283 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1283 was detected is described hereinabove with reference to Figs. 2-8.

[17918] VGAM1283 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Blackcurrant reversion virus. VGAM1283 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17919] VGAM1283 gene, herein designated VGAM GENE, encodes a VGAM1283 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1283 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1283 precursor RNA is designated SEQ ID:33033, and is provided hereinbelow with reference to the sequence listing part.

[17920] VGAM1283 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17921] An enzyme complex designated DICER COMPLEX, dices the VGAM1283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1283 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1283 RNA is designated SEQ ID:33034, and is provided hereinbelow with reference to the sequence listing part.

[17922] VGAM1283 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17923] VGAM1283 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1283 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17924] The complementary binding of VGAM1283 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1283 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17925] It is appreciated that VGAM1283 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1283 host target genes. The mRNA of each one of this plurality of VGAM1283 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1283 RNA, herein designated VGAM RNA, and which when bound by VGAM1283 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1283 host target proteins.

[17926] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1283 gene, herein designated VGAM GENE, on one or more VGAM1283 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17927] It is yet further appreciated that a function of VGAM1283 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of viral infection by Blackcurrant reversion virus. Specific functions, and accordingly utilities, of VGAM1283 correlate with, and may be deduced from, the identity of the host target genes which VGAM1283 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17928] Nucleotide sequences of the VGAM1283 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1283 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1283 are further described hereinbelow with reference to Table 1.

[17929] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1283 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17930] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1284 (VGAM1284) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17931] VGAM1284 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1284 was detected is described hereinabove with reference to Figs. 2–8.

[17932] VGAM1284 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17933] VGAM1284 gene, herein designated VGAM GENE, encodes a VGAM1284 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1284 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1284 precursor RNA is designated SEQ ID:33037, and is provided hereinbelow with reference to the sequence listing part.

[17934] VGAM1284 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17935] An enzyme complex designated DICER COMPLEX, dices the VGAM1284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1284 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1284 RNA is designated SEQ ID:33038, and is provided hereinbelow with reference to the sequence listing part.

[17936] VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17937] VGAM1284 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1284 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1284 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17938] The complementary binding of VGAM1284 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1284 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17939] It is appreciated that VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1284 host target genes. The mRNA of each one of this plurality of VGAM1284 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1284 RNA, herein designated VGAM RNA, and which when bound by VGAM1284 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1284 host target proteins.

[17940] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1284 gene, herein designated VGAM GENE, on one or more VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [17941] It is yet further appreciated that a function of VGAM1284 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1284 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM1284 correlate with, and may be deduced from, the identity of the host target genes which VGAM1284 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [17942] Nucleotide sequences of the VGAM1284 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1284 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1284 are further described hereinbelow with reference to Table 1.
- [17943] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1284 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17944] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1285 (VGAM1285) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17945] VGAM1285 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1285 was detected is described hereinabove with reference to Figs. 2-8.

[17946] VGAM1285 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rice tungro bacilliform virus. VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17947] VGAM1285 gene, herein designated VGAM GENE, encodes a VGAM1285 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1285 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1285 precursor RNA is designated SEQ ID:33043, and is provided hereinbelow with reference to the sequence listing part.

[17948] VGAM1285 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17949] An enzyme complex designated DICER COMPLEX, dices the VGAM1285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1285 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1285 RNA is designated SEQ ID:33044, and is provided hereinbelow with reference to the sequence listing part.

[17950] VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17951] VGAM1285 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1285 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17952] The complementary binding of VGAM1285 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1285 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17953] It is appreciated that VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1285 host target genes. The mRNA of

each one of this plurality of VGAM1285 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1285 RNA, herein designated VGAM RNA, and which when bound by VGAM1285 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1285 host target proteins.

[17954] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1285 gene, herein designated VGAM GENE, on one or more VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[17955] It is yet further appreciated that a function of VGAM1285 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of viral infection by Rice tungro bacilliform virus. Specific functions, and accordingly utilities, of VGAM1285 correlate with, and may be deduced from, the identity of the host target genes which VGAM1285 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17956] Nucleotide sequences of the VGAM1285 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1285 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1285 are further described hereinbelow with reference to Table 1.

[17957] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1285 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[17958] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1286 (VGAM1286) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17959] VGAM1286 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1286 was detected is described hereinabove with reference to Figs. 2–8.

[17960] VGAM1286 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Frog adenovirus 1. VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17961] VGAM1286 gene, herein designated VGAM GENE, encodes a VGAM1286 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1286 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly



similar to the nucleotide sequence of VGAM1286 precursor RNA is designated SEQ ID:33067, and is provided hereinbelow with reference to the sequence listing part.

[17962] VGAM1286 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17963] An enzyme complex designated DICER COMPLEX, dices the VGAM1286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1286 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1286 RNA is designated SEQ ID:33068,

and is provided hereinbelow with reference to the sequence listing part.

[17964] VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17965] VGAM1286 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1286 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17966] The complementary binding of VGAM1286 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1286 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17967] It is appreciated that VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1286 host target genes. The mRNA of each one of this plurality of VGAM1286 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1286 RNA, herein designated VGAM RNA, and which when bound by VGAM1286 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1286 host target proteins.

[17968] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1286 gene, herein designated VGAM GENE, on one or more VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17969] It is yet further appreciated that a function of VGAM1286 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of viral infection by Frog adenovirus 1. Specific functions, and accordingly utilities, of VGAM1286 correlate with, and may be deduced from, the identity of the host target genes which VGAM1286 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17970] Nucleotide sequences of the VGAM1286 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1286 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1286 are further described hereinbelow with reference to Table 1.

[17971] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1286 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17972] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1287 (VGAM1287) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17973] VGAM1287 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1287 was detected is described hereinabove with reference to Figs. 2–8.

[17974] VGAM1287 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1287 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17975] VGAM1287 gene, herein designated VGAM GENE, encodes a VGAM1287 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1287 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1287 precu-

sor RNA is designated SEQ ID:33073, and is provided hereinbelow with reference to the sequence listing part.

[17976] VGAM1287 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17977] An enzyme complex designated DICER COMPLEX, dices the VGAM1287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1287 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1287 RNA is designated SEQ ID:33074, and is provided hereinbelow with reference to the se-

quence listing part.

[17978] VGAM1287 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17979] VGAM1287 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM1287 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17980] The complementary binding of VGAM1287 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1287 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17981] It is appreciated that VGAM1287 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1287 host target genes. The mRNA of each one of this plurality of VGAM1287 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1287 RNA, herein designated VGAM RNA, and which when bound by VGAM1287 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1287 host target proteins.

[17982] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1287 gene, herein designated VGAM GENE, on one or more VGAM1287 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17983] It is yet further appreciated that a function of VGAM1287

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1287 correlate with, and may be deduced from, the identity of the host target genes which VGAM1287 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17984] Nucleotide sequences of the VGAM1287 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1287 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1287 are further described hereinbelow with reference to Table 1.

[17985] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1287 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17986] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1288 (VGAM1288) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17987] VGAM1288 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1288 was detected is described hereinabove with reference to Figs. 2–8.

[17988] VGAM1288 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry vein banding virus. VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17989] VGAM1288 gene, herein designated VGAM GENE, encodes a VGAM1288 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1288 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1288 precursor RNA is designated SEQ ID:33115, and is provided

hereinbelow with reference to the sequence listing part.

[17990] VGAM1288 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17991] An enzyme complex designated DICER COMPLEX, dices the VGAM1288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1288 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1288 RNA is designated SEQ ID:33116, and is provided hereinbelow with reference to the sequence listing part.

[17992] VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[17993] VGAM1288 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1288 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[17994] The complementary binding of VGAM1288 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1288 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17995] It is appreciated that VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1288 host target genes. The mRNA of each one of this plurality of VGAM1288 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1288 RNA, herein designated VGAM RNA, and which when bound by VGAM1288 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1288 host target proteins.

[17996] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1288 gene, herein designated VGAM GENE, on one or more VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[17997] It is yet further appreciated that a function of VGAM1288 is inhibition of expression of host target genes, as part of



a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of viral infection by Strawberry vein banding virus. Specific functions, and accordingly utilities, of VGAM1288 correlate with, and may be deduced from, the identity of the host target genes which VGAM1288 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17998] Nucleotide sequences of the VGAM1288 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1288 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1288 are further described hereinbelow with reference to Table 1.

[17999] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1288 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18000] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1289 (VGAM1289) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18001] VGAM1289 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1289 was detected is described hereinabove with reference to Figs. 2–8.

[18002] VGAM1289 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1289 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18003] VGAM1289 gene, herein designated VGAM GENE, encodes a VGAM1289 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1289 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1289 precursor RNA is designated SEQ ID:33182, and is provided hereinbelow with reference to the sequence listing part.

[18004] VGAM1289 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18005] An enzyme complex designated DICER COMPLEX, dices the VGAM1289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1289 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1289 RNA is designated SEQ ID:33183, and is provided hereinbelow with reference to the sequence listing part.

[18006] VGAM1289 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18007] VGAM1289 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1289 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18008] The complementary binding of VGAM1289 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1289 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18009] It is appreciated that VGAM1289 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1289 host target genes. The mRNA of each one of this plurality of VGAM1289 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1289 RNA, herein designated VGAM

RNA, and which when bound by VGAM1289 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1289 host target proteins.

[18010] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1289 gene, herein designated VGAM GENE, on one or more VGAM1289 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18011] It is yet further appreciated that a function of VGAM1289 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1289 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1289 correlate with, and may be deduced from, the identity of the host target genes which VGAM1289 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18012] Nucleotide sequences of the VGAM1289 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1289 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1289 are further described hereinbelow with reference to Table 1.

[18013] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1289 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18014] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1290 (VGAM1290) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18015] VGAM1290 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1290 was detected is described hereinabove with reference to Figs. 2-8.

[18016] VGAM1290 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid herpesvirus 2. VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18017] VGAM1290 gene, herein designated VGAM GENE, encodes a VGAM1290 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1290 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1290 precursor RNA is designated SEQ ID:33192, and is provided hereinbelow with reference to the sequence listing part.

[18018] VGAM1290 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM1290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18019] An enzyme complex designated DICER COMPLEX, dices the VGAM1290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1290 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1290 RNA is designated SEQ ID:33193, and is provided hereinbelow with reference to the sequence listing part.

[18020] VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18021] VGAM1290 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1290 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1290 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18022] The complementary binding of VGAM1290 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1290 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18023] It is appreciated that VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1290 host target genes. The mRNA of each one of this plurality of VGAM1290 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1290 RNA, herein designated VGAM RNA, and which when bound by VGAM1290 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1290 host target proteins.

[18024] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1290 gene, herein designated VGAM GENE, on one or more VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18025] It is yet further appreciated that a function of VGAM1290 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1290 include diagnosis, prevention and

treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1290 correlate with, and may be deduced from, the identity of the host target genes which VGAM1290 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18026] Nucleotide sequences of the VGAM1290 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1290 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1290 are further described hereinbelow with reference to Table 1.

[18027] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1290 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18028] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1291 (VGAM1291) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18029] VGAM1291 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1291 was detected is described hereinabove with reference to Figs. 2–8.

[18030] VGAM1291 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18031] VGAM1291 gene, herein designated VGAM GENE, encodes a VGAM1291 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1291 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1291 precursor RNA is designated SEQ ID:33195, and is provided hereinbelow with reference to the sequence listing part.

[18032] VGAM1291 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1291 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18033] An enzyme complex designated DICER COMPLEX, dices the VGAM1291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1291 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1291 RNA is designated SEQ ID:33196, and is provided hereinbelow with reference to the sequence listing part.

[18034] VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1291 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18035] VGAM1291 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1291 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18036] The complementary binding of VGAM1291 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1291 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18037] It is appreciated that VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1291 host target genes. The mRNA of each one of this plurality of VGAM1291 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1291 RNA, herein designated VGAM RNA, and which when bound by VGAM1291 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1291 host target proteins.

[18038] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1291 gene, herein designated VGAM GENE, on one or more VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18039] It is yet further appreciated that a function of VGAM1291 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of viral infection by Chimpanzee cy-

tomegalovirus. Specific functions, and accordingly utilities, of VGAM1291 correlate with, and may be deduced from, the identity of the host target genes which VGAM1291 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18040] Nucleotide sequences of the VGAM1291 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1291 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1291 are further described hereinbelow with reference to Table 1.

[18041] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1291 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18042] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1292 (VGAM1292) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[18043] VGAM1292 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1292 was detected is described hereinabove with reference to Figs. 2-8.

[18044] VGAM1292 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee cytomegalovirus. VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18045] VGAM1292 gene, herein designated VGAM GENE, encodes a VGAM1292 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1292 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1292 precursor RNA is designated SEQ ID:33229, and is provided hereinbelow with reference to the sequence listing part.

[18046] VGAM1292 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1292 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18047] An enzyme complex designated DICER COMPLEX, dices the VGAM1292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1292 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1292 RNA is designated SEQ ID:33230, and is provided hereinbelow with reference to the sequence listing part.

[18048] VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1292 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18049] VGAM1292 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1292 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1292 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18050] The complementary binding of VGAM1292 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1292 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18051] It is appreciated that VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1292 host target genes. The mRNA of each one of this plurality of VGAM1292 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1292 RNA, herein designated VGAM RNA, and which when bound by VGAM1292 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1292 host target proteins.

[18052] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1292 gene, herein designated VGAM GENE, on one or more VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18053] It is yet further appreciated that a function of VGAM1292 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1292 include diagnosis, prevention and treatment of viral infection by Chimpanzee cytomegalovirus. Specific functions, and accordingly utili-



ties, of VGAM1292 correlate with, and may be deduced from, the identity of the host target genes which VGAM1292 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18054] Nucleotide sequences of the VGAM1292 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1292 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1292 are further described hereinbelow with reference to Table 1.

[18055] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1292 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18056] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1293 (VGAM1293) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[18057] VGAM1293 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1293 was detected is described hereinabove with reference to Figs. 2–8.

[18058] VGAM1293 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1293 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18059] VGAM1293 gene, herein designated VGAM GENE, encodes a VGAM1293 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1293 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1293 precursor RNA is designated SEQ ID:33236, and is provided hereinbelow with reference to the sequence listing part.

[18060] VGAM1293 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1293 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18061] An enzyme complex designated DICER COMPLEX, dices the VGAM1293 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1293 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1293 RNA is designated SEQ ID:33237, and is provided hereinbelow with reference to the sequence listing part.

[18062] VGAM1293 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1293 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1293 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18063] VGAM1293 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1293 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1293 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1293 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1293 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18064] The complementary binding of VGAM1293 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1293 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1293 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1293 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18065] It is appreciated that VGAM1293 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1293 host target genes. The mRNA of each one of this plurality of VGAM1293 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1293 RNA, herein designated VGAM RNA, and which when bound by VGAM1293 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1293 host target proteins.

[18066] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1293 gene, herein designated VGAM GENE, on one or more VGAM1293 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18067] It is yet further appreciated that a function of VGAM1293 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1293 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1293 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1293 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18068] Nucleotide sequences of the VGAM1293 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1293 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1293 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1293 are further described hereinbelow with reference to Table 1.

[18069] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1293 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18070] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1294 (VGAM1294) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18071] VGAM1294 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1294 was detected is described hereinabove with reference to Figs. 2–8.

[18072] VGAM1294 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18073] VGAM1294 gene, herein designated VGAM GENE, encodes a VGAM1294 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1294 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1294 precursor RNA is designated SEQ ID:33245, and is provided hereinbelow with reference to the sequence listing part.

[18074] VGAM1294 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18075] An enzyme complex designated DICER COMPLEX, dices the VGAM1294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1294 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1294 RNA is designated SEQ ID:33246, and is provided hereinbelow with reference to the sequence listing part.

[18076] VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18077] VGAM1294 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1294 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18078] The complementary binding of VGAM1294 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1294 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18079] It is appreciated that VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1294 host target genes. The mRNA of each one of this plurality of VGAM1294 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1294 RNA, herein designated VGAM RNA, and which when bound by VGAM1294 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1294 host target proteins.

[18080] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1294 gene, herein designated VGAM GENE, on one or more VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18081] It is yet further appreciated that a function of VGAM1294 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1294 correlate with, and may be deduced from, the identity of the host target genes which VGAM1294 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[18082] Nucleotide sequences of the VGAM1294 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1294 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1294 are further described hereinbelow with reference to Table 1.

[18083] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1294 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18084] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1295 (VGAM1295) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18085] VGAM1295 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1295 was detected is described hereinabove with reference to Figs. 2–8.

[18086] VGAM1295 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18087] VGAM1295 gene, herein designated VGAM GENE, encodes a VGAM1295 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1295 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1295 precursor RNA is designated SEQ ID:33251, and is provided hereinbelow with reference to the sequence listing part.

[18088] VGAM1295 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18089] An enzyme complex designated DICER COMPLEX, dices the VGAM1295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1295 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1295 RNA is designated SEQ ID:33252, and is provided hereinbelow with reference to the sequence listing part.

[18090] VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18091] VGAM1295 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1295 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[18092] The complementary binding of VGAM1295 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1295 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18093] It is appreciated that VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1295 host target genes. The mRNA of each one of this plurality of VGAM1295 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1295 RNA, herein designated VGAM RNA, and which when bound by VGAM1295 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1295 host target proteins.

[18094] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1295 gene, herein designated VGAM GENE, on one or more VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18095] It is yet further appreciated that a function of VGAM1295 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1295 correlate with, and may be deduced from, the identity of the host target genes which VGAM1295 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[18096] Nucleotide sequences of the VGAM1295 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1295 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1295 are further described hereinbelow with reference to Table 1.

[18097] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1295 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18098] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1296 (VGAM1296) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18099] VGAM1296 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1296 was detected is described hereinabove with reference to Figs. 2–8.

[18100] VGAM1296 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 4. VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18101] VGAM1296 gene, herein designated VGAM GENE, encodes a VGAM1296 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1296 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1296 precursor RNA is designated SEQ ID:33260, and is provided hereinbelow with reference to the sequence listing part.

[18102] VGAM1296 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18103] An enzyme complex designated DICER COMPLEX, dices the VGAM1296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1296 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1296 RNA is designated SEQ ID:33261, and is provided hereinbelow with reference to the sequence listing part.

[18104] VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[18105] VGAM1296 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1296 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1296 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18106] The complementary binding of VGAM1296 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1296 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18107] It is appreciated that VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1296 host target genes. The mRNA of each one of this plurality of VGAM1296 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1296 RNA, herein designated VGAM RNA, and which when bound by VGAM1296 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1296 host target proteins.

[18108] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1296 gene, herein designated VGAM GENE, on one

or more VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18109] It is yet further appreciated that a function of VGAM1296 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1296 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1296 correlate with, and may be deduced from, the identity of the host target genes which VGAM1296 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[18110] Nucleotide sequences of the VGAM1296 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1296 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1296 are further described hereinbelow with reference to Table 1.

[18111] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1296 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18112] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1297 (VGAM1297) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18113] VGAM1297 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1297 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[18114] VGAM1297 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pea enation mosaic virus–2. VGAM1297 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18115] VGAM1297 gene, herein designated VGAM GENE, encodes a VGAM1297 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1297 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1297 precursor RNA is designated SEQ ID:33281, and is provided hereinbelow with reference to the sequence listing part.

[18116] VGAM1297 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18117] An enzyme complex designated DICER COMPLEX, dices the VGAM1297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1297 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1297 RNA is designated SEQ ID:33282, and is provided hereinbelow with reference to the sequence listing part.

[18118] VGAM1297 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18119] VGAM1297 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1297 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18120] The complementary binding of VGAM1297 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1297 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18121] It is appreciated that VGAM1297 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1297 host target genes. The mRNA of each one of this plurality of VGAM1297 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1297 RNA, herein designated VGAM RNA, and which when bound by VGAM1297 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1297 host target proteins.

[18122] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1297 gene, herein designated VGAM GENE, on one or more VGAM1297 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18123] It is yet further appreciated that a function of VGAM1297 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of viral infection by Pea enation mosaic virus-2. Specific functions, and accordingly utilities, of VGAM1297 correlate with, and may be deduced from, the identity of the host target genes which VGAM1297 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18124] Nucleotide sequences of the VGAM1297 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1297 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1297 are further described hereinbelow with reference to Table 1.

[18125] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1297 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18126] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1298 (VGAM1298) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18127] VGAM1298 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1298 was detected is described hereinabove with reference to Figs. 2-8.

[18128] VGAM1298 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18129] VGAM1298 gene, herein designated VGAM GENE, encodes a VGAM1298 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1298 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1298 precursor RNA is designated SEQ ID:33300, and is provided hereinbelow with reference to the sequence listing part.

[18130] VGAM1298 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[18131] An enzyme complex designated DICER COMPLEX, dices the VGAM1298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1298 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1298 RNA is designated SEQ ID:33301, and is provided hereinbelow with reference to the sequence listing part.

[18132] VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18133] VGAM1298 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1298 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1298 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18134] The complementary binding of VGAM1298 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1298 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18135] It is appreciated that VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1298 host target genes. The mRNA of each one of this plurality of VGAM1298 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1298 RNA, herein designated VGAM RNA, and which when bound by VGAM1298 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1298 host target proteins.

[18136] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1298 gene, herein designated VGAM GENE, on one or more VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18137] It is yet further appreciated that a function of VGAM1298 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1298 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM1298 correlate with, and may be deduced from, the identity of the host target genes which VGAM1298 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18138] Nucleotide sequences of the VGAM1298 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1298 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1298 are further described hereinbelow with reference to Table 1.

[18139] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1298 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18140] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1299 (VGAM1299) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18141] VGAM1299 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1299 was detected is described hereinabove with reference to Figs. 2-8.

[18142] VGAM1299 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of *Macaca mulatta* rhadinovirus. VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18143] VGAM1299 gene, herein designated VGAM GENE, encodes a VGAM1299 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1299 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1299 precursor RNA is designated SEQ ID:33326, and is provided hereinbelow with reference to the sequence listing part.

[18144] VGAM1299 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18145] An enzyme complex designated DICER COMPLEX, dices the VGAM1299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1299 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1299 RNA is designated SEQ ID:33327, and is provided hereinbelow with reference to the sequence listing part.

[18146] VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18147] VGAM1299 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1299 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1299 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18148] The complementary binding of VGAM1299 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1299 host target RNA, herein designated VGAM



HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1299 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18149] It is appreciated that VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1299 host target genes. The mRNA of each one of this plurality of VGAM1299 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1299 RNA, herein designated VGAM RNA, and which when bound by VGAM1299 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1299 host target proteins.

[18150] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1299 gene, herein designated VGAM GENE, on one or more VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18151] It is yet further appreciated that a function of VGAM1299 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1299 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM1299 correlate with, and may be deduced from, the identity of the host target genes which VGAM1299 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18152] Nucleotide sequences of the VGAM1299 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1299 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1299 are further described hereinbelow with reference to Table 1.

[18153] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1299 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18154] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1300 (VGAM1300) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18155] VGAM1300 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1300 was detected is described hereinabove with reference to Figs. 2-8.

[18156] VGAM1300 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Macaca mulatta* rhadi-

novirus. VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18157] VGAM1300 gene, herein designated VGAM GENE, encodes a VGAM1300 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1300 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1300 precursor RNA is designated SEQ ID:33417, and is provided hereinbelow with reference to the sequence listing part.

[18158] VGAM1300 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18159] An enzyme complex designated DICER COMPLEX, dices

the VGAM1300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1300 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1300 RNA is designated SEQ ID:33418, and is provided hereinbelow with reference to the sequence listing part.

[18160] VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18161] VGAM1300 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1300 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1300 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18162] The complementary binding of VGAM1300 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1300 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18163] It is appreciated that VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1300 host target genes. The mRNA of each one of this plurality of VGAM1300 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1300 RNA, herein designated VGAM RNA, and which when bound by VGAM1300 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1300 host target proteins.

[18164] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1300 gene, herein designated VGAM GENE, on one or more VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18165] It is yet further appreciated that a function of VGAM1300 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM1300 correlate with, and may be deduced from, the identity of the host target genes which VGAM1300 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18166] Nucleotide sequences of the VGAM1300 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1300 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM1300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1300 are further described hereinbelow with reference to Table 1.

[18167] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1300 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18168] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1301 (VGAM1301) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18169] VGAM1301 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1301 was detected is described hereinabove with reference to Figs. 2-8.

[18170] VGAM1301 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM1301 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18171] VGAM1301 gene, herein designated VGAM GENE, encodes a VGAM1301 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1301 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1301 precursor RNA is designated SEQ ID:33438, and is provided hereinbelow with reference to the sequence listing part.

[18172] VGAM1301 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1301 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18173] An enzyme complex designated DICER COMPLEX, dices the VGAM1301 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1301 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1301 RNA is designated SEQ ID:33439, and is provided hereinbelow with reference to the sequence listing part.

[18174] VGAM1301 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18175] VGAM1301 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1301 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1301 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18176] The complementary binding of VGAM1301 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1301

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1301 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18177] It is appreciated that VGAM1301 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1301 host target genes. The mRNA of each one of this plurality of VGAM1301 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1301 RNA, herein designated VGAM RNA, and which when bound by VGAM1301 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1301 host target proteins.

[18178] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1301 gene, herein designated VGAM GENE, on one or more VGAM1301 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18179] It is yet further appreciated that a function of VGAM1301 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1301 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM1301 correlate with, and may be deduced from, the identity of the host target genes which VGAM1301 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18180] Nucleotide sequences of the VGAM1301 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1301 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1301 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1301 are further described hereinbelow with reference to Table 1.

[18181] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1301 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18182] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1302 (VGAM1302) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18183] VGAM1302 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1302 was detected is described hereinabove with reference to Figs. 2-8.

[18184] VGAM1302 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[18185] VGAM1302 gene, herein designated VGAM GENE, encodes a VGAM1302 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1302 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1302 precursor RNA is designated SEQ ID:33461, and is provided hereinbelow with reference to the sequence listing part.

[18186] VGAM1302 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18187] An enzyme complex designated DICER COMPLEX, dices the VGAM1302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1302 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1302 RNA is designated SEQ ID:33462, and is provided hereinbelow with reference to the sequence listing part.

[18188] VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18189] VGAM1302 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1302 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1302 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18190] The complementary binding of VGAM1302 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1302 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1302 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18191] It is appreciated that VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1302 host target genes. The mRNA of each one of this plurality of VGAM1302 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1302 RNA, herein designated VGAM RNA, and which when bound by VGAM1302 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1302 host target proteins.

[18192] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1302 gene, herein designated VGAM GENE, on one or more VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18193] It is yet further appreciated that a function of VGAM1302 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1302 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM1302 correlate with, and may be deduced from, the identity of the host target genes which VGAM1302 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18194] Nucleotide sequences of the VGAM1302 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1302 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1302 are further

described hereinbelow with reference to Table 1.

[18195] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1302 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18196] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1303 (VGAM1303) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18197] VGAM1303 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1303 was detected is described hereinabove with reference to Figs. 2-8.

[18198] VGAM1303 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca mulatta rhadinovirus. VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18199] VGAM1303 gene, herein designated VGAM GENE, encodes a VGAM1303 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1303 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1303 precursor RNA is designated SEQ ID:33465, and is provided hereinbelow with reference to the sequence listing part.

[18200] VGAM1303 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18201] An enzyme complex designated DICER COMPLEX, dices the VGAM1303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1303 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1303 RNA is designated SEQ ID:33466, and is provided hereinbelow with reference to the sequence listing part.

[18202] VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18203] VGAM1303 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1303 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1303 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18204] The complementary binding of VGAM1303 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1303 host target protein, herein desig-



nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18205] It is appreciated that VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1303 host target genes. The mRNA of each one of this plurality of VGAM1303 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1303 RNA, herein designated VGAM RNA, and which when bound by VGAM1303 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1303 host target proteins.

[18206] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1303 gene, herein designated VGAM GENE, on one or more VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18207] It is yet further appreciated that a function of VGAM1303 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of viral infection by *Macaca mulatta* rhadinovirus. Specific functions, and accordingly utilities, of VGAM1303 correlate with, and may be deduced from, the identity of the host target genes which VGAM1303 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18208] Nucleotide sequences of the VGAM1303 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1303 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1303 are further described hereinbelow with reference to Table 1.

[18209] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1303 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18210] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1304 (VGAM1304) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18211] VGAM1304 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1304 was detected is described hereinabove with reference to Figs. 2-8.

[18212] VGAM1304 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rhesus monkey papillomavirus. VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18213] VGAM1304 gene, herein designated VGAM GENE, encodes

a VGAM1304 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1304 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1304 precursor RNA is designated SEQ ID:33476, and is provided hereinbelow with reference to the sequence listing part.

[18214] VGAM1304 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18215] An enzyme complex designated DICER COMPLEX, dices the VGAM1304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1304 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1304 RNA is designated SEQ ID:33477, and is provided hereinbelow with reference to the sequence listing part.

[18216] VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18217] VGAM1304 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1304 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1304 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18218] The complementary binding of VGAM1304 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1304 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[18219] It is appreciated that VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1304 host target genes. The mRNA of each one of this plurality of VGAM1304 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1304 RNA, herein designated VGAM RNA, and which when bound by VGAM1304 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1304 host target proteins.

[18220] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1304 gene, herein designated VGAM GENE, on one or more VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18221] It is yet further appreciated that a function of VGAM1304 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1304 include diagnosis, prevention and treatment of viral infection by Rhesus monkey papillomavirus. Specific functions, and accordingly utilities, of VGAM1304 correlate with, and may be deduced from, the identity of the host target genes which VGAM1304 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18222] Nucleotide sequences of the VGAM1304 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1304 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1304 are further described hereinbelow with reference to Table 1.

[18223] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1304 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18224] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1305 (VGAM1305) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18225] VGAM1305 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1305 was detected is described hereinabove with reference to Figs. 2-8.

[18226] VGAM1305 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Paramecium bursaria Chlorella virus 1. VGAM1305 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18227] VGAM1305 gene, herein designated VGAM GENE, encodes a VGAM1305 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1305 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1305 precursor RNA is designated SEQ ID:33483, and is provided hereinbelow with reference to the sequence listing part.

[18228] VGAM1305 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18229] An enzyme complex designated DICER COMPLEX, dices the VGAM1305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1305 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1305 RNA is designated SEQ ID:33484, and is provided hereinbelow with reference to the sequence listing part.

[18230] VGAM1305 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18231] VGAM1305 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1305 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18232] The complementary binding of VGAM1305 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1305 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18233] It is appreciated that VGAM1305 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1305 host target genes. The mRNA of each one of this plurality of VGAM1305 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1305 RNA, herein designated VGAM RNA, and which when bound by VGAM1305 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1305 host target proteins.

[18234] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1305 gene, herein designated VGAM GENE, on one or more VGAM1305 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18235] It is yet further appreciated that a function of VGAM1305 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of viral infection by Paramecium bursaria Chlorella virus 1. Specific functions, and accordingly utilities, of VGAM1305 correlate with, and may be deduced from, the identity of the host target genes which VGAM1305 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18236] Nucleotide sequences of the VGAM1305 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1305 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1305 are further described hereinbelow with reference to Table 1.

[18237] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1305 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18238] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1306 (VGAM1306) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18239] VGAM1306 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1306 was detected is described hereinabove with reference to Figs. 2-8.

[18240] VGAM1306 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1306 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18241] VGAM1306 gene, herein designated VGAM GENE, encodes a VGAM1306 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1306 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1306 precursor RNA is designated SEQ ID:33488, and is provided hereinbelow with reference to the sequence listing part.

[18242] VGAM1306 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18243] An enzyme complex designated DICER COMPLEX, dices the VGAM1306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1306 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1306 RNA is designated SEQ ID:33489, and is provided hereinbelow with reference to the sequence listing part.

[18244] VGAM1306 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18245] VGAM1306 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1306 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18246] The complementary binding of VGAM1306 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1306 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18247] It is appreciated that VGAM1306 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1306 host target genes. The mRNA of each one of this plurality of VGAM1306 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1306 RNA, herein designated VGAM RNA, and which when bound by VGAM1306 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1306 host target proteins.

[18248] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1306 gene, herein designated VGAM GENE, on one or more VGAM1306 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18249] It is yet further appreciated that a function of VGAM1306 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM1306 correlate with, and may be deduced from, the identity of the host target genes which VGAM1306 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18250] Nucleotide sequences of the VGAM1306 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1306 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1306 are further described hereinbelow with reference to Table 1.

[18251] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1306 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18252] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1307 (VGAM1307) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18253] VGAM1307 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1307 was detected is described hereinabove with reference to Figs. 2–8.

[18254] VGAM1307 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus A. VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18255] VGAM1307 gene, herein designated VGAM GENE, encodes a VGAM1307 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1307 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1307 precursor RNA is designated SEQ ID:33528, and is provided hereinbelow with reference to the sequence listing part.

[18256] VGAM1307 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18257] An enzyme complex designated DICER COMPLEX, dices the VGAM1307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1307 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1307 RNA is designated SEQ ID:33529, and is provided hereinbelow with reference to the sequence listing part.

[18258] VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18259] VGAM1307 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1307 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1307 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18260] The complementary binding of VGAM1307 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1307 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18261] It is appreciated that VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1307 host target genes. The mRNA of each one of this plurality of VGAM1307 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1307 RNA, herein designated VGAM RNA, and which when bound by VGAM1307 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1307 host target proteins.

[18262] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1307 gene, herein designated VGAM GENE, on one or more VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [18263] It is yet further appreciated that a function of VGAM1307 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1307 include diagnosis, prevention and treatment of viral infection by Human adenovirus A. Specific functions, and accordingly utilities, of VGAM1307 correlate with, and may be deduced from, the identity of the host target genes which VGAM1307 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [18264] Nucleotide sequences of the VGAM1307 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1307 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1307 are further described hereinbelow with reference to Table 1.
- [18265] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1307 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18266] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1308 (VGAM1308) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18267] VGAM1308 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1308 was detected is described hereinabove with reference to Figs. 2–8.

[18268] VGAM1308 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus A. VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18269] VGAM1308 gene, herein designated VGAM GENE, encodes a VGAM1308 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1308 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1308 precursor RNA is designated SEQ ID:33541, and is provided hereinbelow with reference to the sequence listing part.

[18270] VGAM1308 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18271] An enzyme complex designated DICER COMPLEX, dices the VGAM1308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1308 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM1308 RNA is designated SEQ ID:33542, and is provided hereinbelow with reference to the sequence listing part.

[18272] VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18273] VGAM1308 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1308 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18274] The complementary binding of VGAM1308 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1308 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18275] It is appreciated that VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1308 host target genes. The mRNA of

each one of this plurality of VGAM1308 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1308 RNA, herein designated VGAM RNA, and which when bound by VGAM1308 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1308 host target proteins.

[18276] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1308 gene, herein designated VGAM GENE, on one or more VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[18277] It is yet further appreciated that a function of VGAM1308 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of viral infection by Human adenovirus A. Specific functions, and accordingly utilities, of VGAM1308 correlate with, and may be deduced from, the identity of the host target genes which VGAM1308 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18278] Nucleotide sequences of the VGAM1308 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1308 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1308 are further described hereinbelow with reference to Table 1.

[18279] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1308 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[18280] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1309 (VGAM1309) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18281] VGAM1309 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1309 was detected is described hereinabove with reference to Figs. 2–8.

[18282] VGAM1309 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus A. VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18283] VGAM1309 gene, herein designated VGAM GENE, encodes a VGAM1309 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1309 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1309 precursor RNA is designated SEQ ID:33547, and is provided hereinbelow with reference to the sequence listing part.

[18284] VGAM1309 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18285] An enzyme complex designated DICER COMPLEX, dices the VGAM1309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1309 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1309 RNA is designated SEQ ID:33548,

and is provided hereinbelow with reference to the sequence listing part.

[18286] VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18287] VGAM1309 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1309 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18288] The complementary binding of VGAM1309 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1309 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18289] It is appreciated that VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1309 host target genes. The mRNA of each one of this plurality of VGAM1309 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1309 RNA, herein designated VGAM RNA, and which when bound by VGAM1309 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1309 host target proteins.

[18290] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1309 gene, herein designated VGAM GENE, on one or more VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18291] It is yet further appreciated that a function of VGAM1309 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of viral infection by Human adenovirus A. Specific functions, and accordingly utilities, of VGAM1309 correlate with, and may be deduced from, the identity of the host target genes which VGAM1309 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18292] Nucleotide sequences of the VGAM1309 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1309 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1309 are further described hereinbelow with reference to Table 1.

[18293] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1309 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18294] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1310 (VGAM1310) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18295] VGAM1310 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1310 was detected is described hereinabove with reference to Figs. 2–8.

[18296] VGAM1310 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus A. VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18297] VGAM1310 gene, herein designated VGAM GENE, encodes a VGAM1310 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1310 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1310 precursor

sor RNA is designated SEQ ID:33553, and is provided hereinbelow with reference to the sequence listing part.

[18298] VGAM1310 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18299] An enzyme complex designated DICER COMPLEX, dices the VGAM1310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1310 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1310 RNA is designated SEQ ID:33554, and is provided hereinbelow with reference to the se-



quence listing part.

[18300] VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18301] VGAM1310 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1310 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18302] The complementary binding of VGAM1310 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1310 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18303] It is appreciated that VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1310 host target genes. The mRNA of each one of this plurality of VGAM1310 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1310 RNA, herein designated VGAM RNA, and which when bound by VGAM1310 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1310 host target proteins.

[18304] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1310 gene, herein designated VGAM GENE, on one or more VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18305] It is yet further appreciated that a function of VGAM1310

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of viral infection by Human adenovirus A. Specific functions, and accordingly utilities, of VGAM1310 correlate with, and may be deduced from, the identity of the host target genes which VGAM1310 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18306] Nucleotide sequences of the VGAM1310 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1310 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1310 are further described hereinbelow with reference to Table 1.

[18307] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1310 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18308] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1311 (VGAM1311) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18309] VGAM1311 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1311 was detected is described hereinabove with reference to Figs. 2–8.

[18310] VGAM1311 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18311] VGAM1311 gene, herein designated VGAM GENE, encodes a VGAM1311 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1311 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1311 precursor RNA is designated SEQ ID:33591, and is provided

hereinbelow with reference to the sequence listing part.

[18312] VGAM1311 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18313] An enzyme complex designated DICER COMPLEX, dices the VGAM1311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1311 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1311 RNA is designated SEQ ID:33592, and is provided hereinbelow with reference to the sequence listing part.

[18314] VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18315] VGAM1311 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1311 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18316] The complementary binding of VGAM1311 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1311 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18317] It is appreciated that VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1311 host target genes. The mRNA of each one of this plurality of VGAM1311 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM1311 RNA, herein designated VGAM RNA, and which when bound by VGAM1311 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1311 host target proteins.

[18318] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1311 gene, herein designated VGAM GENE, on one or more VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18319] It is yet further appreciated that a function of VGAM1311 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM1311 correlate with, and may be deduced from, the identity of the host target genes which VGAM1311 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18320] Nucleotide sequences of the VGAM1311 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1311 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1311 are further described hereinbelow with reference to Table 1.

[18321] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1311 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18322] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1312 (VGAM1312) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18323] VGAM1312 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1312 was detected is described hereinabove with reference to Figs. 2–8.

[18324] VGAM1312 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African swine fever virus. VGAM1312 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18325] VGAM1312 gene, herein designated VGAM GENE, encodes a VGAM1312 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1312 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1312 precursor RNA is designated SEQ ID:33594, and is provided hereinbelow with reference to the sequence listing part.

[18326] VGAM1312 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18327] An enzyme complex designated DICER COMPLEX, dices the VGAM1312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1312 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1312 RNA is designated SEQ ID:33595, and is provided hereinbelow with reference to the sequence listing part.

[18328] VGAM1312 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18329] VGAM1312 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1312 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18330] The complementary binding of VGAM1312 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1312 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18331] It is appreciated that VGAM1312 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1312 host target genes. The mRNA of each one of this plurality of VGAM1312 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1312 RNA, herein designated VGAM

RNA, and which when bound by VGAM1312 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1312 host target proteins.

[18332] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1312 gene, herein designated VGAM GENE, on one or more VGAM1312 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18333] It is yet further appreciated that a function of VGAM1312 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1312 include diagnosis, prevention and treatment of viral infection by African swine fever virus. Specific functions, and accordingly utilities, of VGAM1312 correlate with, and may be deduced from, the identity of the host target genes which VGAM1312 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18334] Nucleotide sequences of the VGAM1312 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1312 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1312 are further described hereinbelow with reference to Table 1.

[18335] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1312 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18336] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 1313 (VGAM1313) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18337] VGAM1313 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1313 was detected is described hereinabove with reference to Figs. 2-8.

[18338] VGAM1313 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine herpesvirus 7. VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18339] VGAM1313 gene, herein designated VGAM GENE, encodes a VGAM1313 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1313 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1313 precursor RNA is designated SEQ ID:33634, and is provided hereinbelow with reference to the sequence listing part.

[18340] VGAM1313 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18341] An enzyme complex designated DICER COMPLEX, dices the VGAM1313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1313 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1313 RNA is designated SEQ ID:33635, and is provided hereinbelow with reference to the sequence listing part.

[18342] VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18343] VGAM1313 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1313 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1313 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18344] The complementary binding of VGAM1313 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1313 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18345] It is appreciated that VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1313 host target genes. The mRNA of each one of this plurality of VGAM1313 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1313 RNA, herein designated VGAM RNA, and which when bound by VGAM1313 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1313 host target proteins.

[18346] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1313 gene, herein designated VGAM GENE, on one or more VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18347] It is yet further appreciated that a function of VGAM1313 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1313 include diagnosis, prevention and

treatment of viral infection by Cercopithecine herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1313 correlate with, and may be deduced from, the identity of the host target genes which VGAM1313 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18348] Nucleotide sequences of the VGAM1313 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1313 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1313 are further described hereinbelow with reference to Table 1.

[18349] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1313 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18350] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1314 (VGAM1314) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18351] VGAM1314 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1314 was detected is described hereinabove with reference to Figs. 2–8.

[18352] VGAM1314 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18353] VGAM1314 gene, herein designated VGAM GENE, encodes a VGAM1314 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1314 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1314 precursor RNA is designated SEQ ID:33639, and is provided hereinbelow with reference to the sequence listing part.

[18354] VGAM1314 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1314 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18355] An enzyme complex designated DICER COMPLEX, dices the VGAM1314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1314 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1314 RNA is designated SEQ ID:33640, and is provided hereinbelow with reference to the sequence listing part.

[18356] VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1314 host target RNA, herein designated



VGAM HOST TARGET RNA. VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18357] VGAM1314 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1314 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18358] The complementary binding of VGAM1314 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1314 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18359] It is appreciated that VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1314 host target genes. The mRNA of each one of this plurality of VGAM1314 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1314 RNA, herein designated VGAM RNA, and which when bound by VGAM1314 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1314 host target proteins.

[18360] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1314 gene, herein designated VGAM GENE, on one or more VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18361] It is yet further appreciated that a function of VGAM1314 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM1314 correlate with, and may be deduced from, the identity of the host target genes which VGAM1314 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18362] Nucleotide sequences of the VGAM1314 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1314 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1314 are further described hereinbelow with reference to Table 1.

[18363] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1314 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18364] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1315 (VGAM1315) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18365] VGAM1315 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1315 was detected is described hereinabove with reference to Figs. 2–8.

[18366] VGAM1315 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus B. VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18367] VGAM1315 gene, herein designated VGAM GENE, encodes a VGAM1315 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1315 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1315 precu-

sor RNA is designated SEQ ID:33643, and is provided hereinbelow with reference to the sequence listing part.

[18368] VGAM1315 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18369] An enzyme complex designated DICER COMPLEX, dices the VGAM1315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1315 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1315 RNA is designated SEQ ID:33644, and is provided hereinbelow with reference to the se-

quence listing part.

[18370] VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18371] VGAM1315 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1315 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18372] The complementary binding of VGAM1315 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1315 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18373] It is appreciated that VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1315 host target genes. The mRNA of each one of this plurality of VGAM1315 host target genes comprises one or more host target binding sites, each



having a nucleotide sequence which is at least partly complementary to VGAM1315 RNA, herein designated VGAM RNA, and which when bound by VGAM1315 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1315 host target proteins.

[18374] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1315 gene, herein designated VGAM GENE, on one or more VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18375] It is yet further appreciated that a function of VGAM1315

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of viral infection by Human adenovirus B. Specific functions, and accordingly utilities, of VGAM1315 correlate with, and may be deduced from, the identity of the host target genes which VGAM1315 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18376] Nucleotide sequences of the VGAM1315 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1315 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1315 are further described hereinbelow with reference to Table 1.

[18377] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1315 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18378] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1316 (VGAM1316) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18379] VGAM1316 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1316 was detected is described hereinabove with reference to Figs. 2–8.

[18380] VGAM1316 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia virus. VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18381] VGAM1316 gene, herein designated VGAM GENE, encodes a VGAM1316 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1316 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1316 precursor RNA is designated SEQ ID:33675, and is provided

hereinbelow with reference to the sequence listing part.

[18382] VGAM1316 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18383] An enzyme complex designated DICER COMPLEX, dices the VGAM1316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1316 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1316 RNA is designated SEQ ID:33676, and is provided hereinbelow with reference to the sequence listing part.

[18384] VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18385] VGAM1316 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1316 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18386] The complementary binding of VGAM1316 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1316 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18387] It is appreciated that VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1316 host target genes. The mRNA of each one of this plurality of VGAM1316 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1316 RNA, herein designated VGAM RNA, and which when bound by VGAM1316 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1316 host target proteins.

[18388] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1316 gene, herein designated VGAM GENE, on one or more VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18389] It is yet further appreciated that a function of VGAM1316 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of viral infection by Vaccinia virus. Specific functions, and accordingly utilities, of VGAM1316 correlate with, and may be deduced from, the identity of the host target genes which VGAM1316 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18390] Nucleotide sequences of the VGAM1316 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1316 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1316 are further described hereinbelow with reference to Table 1.

[18391] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1316 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18392] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present



invention, referred to here as Viral Genomic Address Messenger 1317 (VGAM1317) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18393] VGAM1317 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1317 was detected is described hereinabove with reference to Figs. 2–8.

[18394] VGAM1317 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like disease virus. VGAM1317 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18395] VGAM1317 gene, herein designated VGAM GENE, encodes a VGAM1317 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1317 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1317 precursor RNA is designated SEQ ID:33701, and is provided hereinbelow with reference to the sequence listing part.

[18396] VGAM1317 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18397] An enzyme complex designated DICER COMPLEX, dices the VGAM1317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1317 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1317 RNA is designated SEQ ID:33702, and is provided hereinbelow with reference to the sequence listing part.

[18398] VGAM1317 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18399] VGAM1317 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1317 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18400] The complementary binding of VGAM1317 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1317 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18401] It is appreciated that VGAM1317 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1317 host target genes. The mRNA of each one of this plurality of VGAM1317 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1317 RNA, herein designated VGAM

RNA, and which when bound by VGAM1317 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1317 host target proteins.

[18402] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1317 gene, herein designated VGAM GENE, on one or more VGAM1317 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18403] It is yet further appreciated that a function of VGAM1317 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1317 include diagnosis, prevention and treatment of viral infection by Yaba-like disease virus. Specific functions, and accordingly utilities, of VGAM1317 correlate with, and may be deduced from, the identity of the host target genes which VGAM1317 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18404] Nucleotide sequences of the VGAM1317 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1317 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1317 are further described hereinbelow with reference to Table 1.

[18405] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1317 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18406] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1318 (VGAM1318) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18407] VGAM1318 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1318 was detected is described hereinabove with reference to Figs. 2–8.

[18408] VGAM1318 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine enterovirus B. VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18409] VGAM1318 gene, herein designated VGAM GENE, encodes a VGAM1318 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1318 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1318 precursor RNA is designated SEQ ID:33708, and is provided hereinbelow with reference to the sequence listing part.

[18410] VGAM1318 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18411] An enzyme complex designated DICER COMPLEX, dices the VGAM1318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1318 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1318 RNA is designated SEQ ID:33709, and is provided hereinbelow with reference to the sequence listing part.

[18412] VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger



RNA, VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18413] VGAM1318 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1318 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1318 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1318 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18414] The complementary binding of VGAM1318 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1318 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18415] It is appreciated that VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1318 host target genes. The mRNA of each one of this plurality of VGAM1318 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1318 RNA, herein designated VGAM RNA, and which when bound by VGAM1318 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1318 host target proteins.

[18416] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1318 gene, herein designated VGAM GENE, on one or more VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18417] It is yet further appreciated that a function of VGAM1318 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1318 include diagnosis, prevention and

treatment of viral infection by Porcine enterovirus B. Specific functions, and accordingly utilities, of VGAM1318 correlate with, and may be deduced from, the identity of the host target genes which VGAM1318 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18418] Nucleotide sequences of the VGAM1318 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1318 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1318 are further described hereinbelow with reference to Table 1.

[18419] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1318 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18420] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1319 (VGAM1319) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18421] VGAM1319 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1319 was detected is described hereinabove with reference to Figs. 2–8.

[18422] VGAM1319 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like disease virus. VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18423] VGAM1319 gene, herein designated VGAM GENE, encodes a VGAM1319 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1319 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1319 precursor RNA is designated SEQ ID:33716, and is provided hereinbelow with reference to the sequence listing part.

[18424] VGAM1319 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1319 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18425] An enzyme complex designated DICER COMPLEX, dices the VGAM1319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1319 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1319 RNA is designated SEQ ID:33717, and is provided hereinbelow with reference to the sequence listing part.

[18426] VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1319 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18427] VGAM1319 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1319 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18428] The complementary binding of VGAM1319 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1319 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18429] It is appreciated that VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1319 host target genes. The mRNA of each one of this plurality of VGAM1319 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1319 RNA, herein designated VGAM RNA, and which when bound by VGAM1319 RNA, herein designated VGAM RNA, causes inhibition of translation of



respective one or more VGAM1319 host target proteins.

[18430] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1319 gene, herein designated VGAM GENE, on one or more VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18431] It is yet further appreciated that a function of VGAM1319 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of viral infection by Yaba-like disease virus.

Specific functions, and accordingly utilities, of VGAM1319 correlate with, and may be deduced from, the identity of the host target genes which VGAM1319 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18432] Nucleotide sequences of the VGAM1319 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1319 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1319 are further described hereinbelow with reference to Table 1.

[18433] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1319 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18434] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1320 (VGAM1320) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[18435] VGAM1320 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1320 was detected is described hereinabove with reference to Figs. 2–8.

[18436] VGAM1320 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18437] VGAM1320 gene, herein designated VGAM GENE, encodes a VGAM1320 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1320 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1320 precursor RNA is designated SEQ ID:33759, and is provided hereinbelow with reference to the sequence listing part.

[18438] VGAM1320 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1320 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18439] An enzyme complex designated DICER COMPLEX, dices the VGAM1320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1320 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1320 RNA is designated SEQ ID:33760, and is provided hereinbelow with reference to the sequence listing part.

[18440] VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1320 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18441] VGAM1320 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1320 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1320 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18442] The complementary binding of VGAM1320 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1320 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18443] It is appreciated that VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1320 host target genes. The mRNA of each one of this plurality of VGAM1320 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1320 RNA, herein designated VGAM RNA, and which when bound by VGAM1320 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1320 host target proteins.

[18444] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1320 gene, herein designated VGAM GENE, on one or more VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18445] It is yet further appreciated that a function of VGAM1320 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1320 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities,

of VGAM1320 correlate with, and may be deduced from, the identity of the host target genes which VGAM1320 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18446] Nucleotide sequences of the VGAM1320 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1320 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1320 are further described hereinbelow with reference to Table 1.

[18447] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1320 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18448] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1321 (VGAM1321) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the



art.

[18449] VGAM1321 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1321 was detected is described hereinabove with reference to Figs. 2–8.

[18450] VGAM1321 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18451] VGAM1321 gene, herein designated VGAM GENE, encodes a VGAM1321 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1321 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1321 precursor RNA is designated SEQ ID:33767, and is provided hereinbelow with reference to the sequence listing part.

[18452] VGAM1321 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18453] An enzyme complex designated DICER COMPLEX, dices the VGAM1321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1321 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1321 RNA is designated SEQ ID:33768, and is provided hereinbelow with reference to the sequence listing part.

[18454] VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18455] VGAM1321 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1321 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18456] The complementary binding of VGAM1321 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1321 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18457] It is appreciated that VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1321 host target genes. The mRNA of each one of this plurality of VGAM1321 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1321 RNA, herein designated VGAM RNA, and which when bound by VGAM1321 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1321 host target proteins.

[18458] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1321 gene, herein designated VGAM GENE, on one or more VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18459] It is yet further appreciated that a function of VGAM1321 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1321 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1321 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18460] Nucleotide sequences of the VGAM1321 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1321 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1321 are further described hereinbelow with reference to Table 1.

[18461] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1321 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18462] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1322 (VGAM1322) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18463] VGAM1322 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1322 was detected is described hereinabove with reference to Figs. 2–8.

[18464] VGAM1322 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18465] VGAM1322 gene, herein designated VGAM GENE, encodes a VGAM1322 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1322 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1322 precursor RNA is designated SEQ ID:33770, and is provided hereinbelow with reference to the sequence listing part.

[18466] VGAM1322 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18467] An enzyme complex designated DICER COMPLEX, dices the VGAM1322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1322 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1322 RNA is designated SEQ ID:33771, and is provided hereinbelow with reference to the sequence listing part.

[18468] VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding



gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18469] VGAM1322 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1322 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18470] The complementary binding of VGAM1322 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1322 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18471] It is appreciated that VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1322 host target genes. The mRNA of each one of this plurality of VGAM1322 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1322 RNA, herein designated VGAM RNA, and which when bound by VGAM1322 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1322 host target proteins.

[18472] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1322 gene, herein designated VGAM GENE, on one or more VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18473] It is yet further appreciated that a function of VGAM1322 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1322 correlate with, and may be deduced from, the identity of the host target genes which VGAM1322

binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18474] Nucleotide sequences of the VGAM1322 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1322 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1322 are further described hereinbelow with reference to Table 1.

[18475] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1322 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18476] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1323 (VGAM1323) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18477] VGAM1323 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1323 was detected is described hereinabove with reference to Figs. 2–8.

[18478] VGAM1323 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18479] VGAM1323 gene, herein designated VGAM GENE, encodes a VGAM1323 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1323 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1323 precursor RNA is designated SEQ ID:33775, and is provided hereinbelow with reference to the sequence listing part.

[18480] VGAM1323 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18481] An enzyme complex designated DICER COMPLEX, dices the VGAM1323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1323 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1323 RNA is designated SEQ ID:33776, and is provided hereinbelow with reference to the sequence listing part.

[18482] VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18483] VGAM1323 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1323 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[18484] The complementary binding of VGAM1323 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1323 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18485] It is appreciated that VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1323 host target genes. The mRNA of each one of this plurality of VGAM1323 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1323 RNA, herein designated VGAM RNA, and which when bound by VGAM1323 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1323 host target proteins.

[18486] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by



VGAM1323 gene, herein designated VGAM GENE, on one or more VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18487] It is yet further appreciated that a function of VGAM1323 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1323 correlate with, and may be deduced from, the identity of the host target genes which VGAM1323 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[18488] Nucleotide sequences of the VGAM1323 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1323 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1323 are further described hereinbelow with reference to Table 1.

[18489] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1323 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18490] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1324 (VGAM1324) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18491] VGAM1324 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1324 was detected is described hereinabove with reference to Figs. 2–8.

[18492] VGAM1324 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18493] VGAM1324 gene, herein designated VGAM GENE, encodes a VGAM1324 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1324 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1324 precursor RNA is designated SEQ ID:33840, and is provided hereinbelow with reference to the sequence listing part.

[18494] VGAM1324 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18495] An enzyme complex designated DICER COMPLEX, dices the VGAM1324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1324 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1324 RNA is designated SEQ ID:33841, and is provided hereinbelow with reference to the sequence listing part.

[18496] VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[18497] VGAM1324 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1324 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18498] The complementary binding of VGAM1324 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1324 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18499] It is appreciated that VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1324 host target genes. The mRNA of each one of this plurality of VGAM1324 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1324 RNA, herein designated VGAM RNA, and which when bound by VGAM1324 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1324 host target proteins.

[18500] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1324 gene, herein designated VGAM GENE, on one

or more VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18501] It is yet further appreciated that a function of VGAM1324 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1324 correlate with, and may be deduced from, the identity of the host target genes which VGAM1324 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18502] Nucleotide sequences of the VGAM1324 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1324 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1324 are further described hereinbelow with reference to Table 1.

[18503] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1324 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18504] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1325 (VGAM1325) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18505] VGAM1325 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1325 was detected is de-



scribed hereinabove with reference to Figs. 2–8.

[18506] VGAM1325 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human foamy virus.

VGAM1325 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18507] VGAM1325 gene, herein designated VGAM GENE, encodes a VGAM1325 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1325 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1325 precursor RNA is designated SEQ ID:33844, and is provided hereinbelow with reference to the sequence listing part.

[18508] VGAM1325 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18509] An enzyme complex designated DICER COMPLEX, dices the VGAM1325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1325 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1325 RNA is designated SEQ ID:31898, and is provided hereinbelow with reference to the sequence listing part.

[18510] VGAM1325 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18511] VGAM1325 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1325 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1325 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18512] The complementary binding of VGAM1325 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1325 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18513] It is appreciated that VGAM1325 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1325 host target genes. The mRNA of each one of this plurality of VGAM1325 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1325 RNA, herein designated VGAM RNA, and which when bound by VGAM1325 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1325 host target proteins.

[18514] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1325 gene, herein designated VGAM GENE, on one or more VGAM1325 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18515] It is yet further appreciated that a function of VGAM1325 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1325 include diagnosis, prevention and treatment of viral infection by Human foamy virus. Specific functions, and accordingly utilities, of VGAM1325 correlate with, and may be deduced from, the identity of the host target genes which VGAM1325 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18516] Nucleotide sequences of the VGAM1325 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1325 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1325 are further described hereinbelow with reference to Table 1.

[18517] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1325 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18518] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1326 (VGAM1326) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18519] VGAM1326 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1326 was detected is described hereinabove with reference to Figs. 2-8.

[18520] VGAM1326 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18521] VGAM1326 gene, herein designated VGAM GENE, encodes a VGAM1326 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1326 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1326 precursor RNA is designated SEQ ID:33845, and is provided hereinbelow with reference to the sequence listing part.

[18522] VGAM1326 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[18523] An enzyme complex designated DICER COMPLEX, dices the VGAM1326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1326 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1326 RNA is designated SEQ ID:33846, and is provided hereinbelow with reference to the sequence listing part.

[18524] VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18525] VGAM1326 RNA, herein designated VGAM RNA, binds



complementarily to one or more host target binding sites located in untranslated regions of VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1326 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18526] The complementary binding of VGAM1326 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1326 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18527] It is appreciated that VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1326 host target genes. The mRNA of each one of this plurality of VGAM1326 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1326 RNA, herein designated VGAM RNA, and which when bound by VGAM1326 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1326 host target proteins.

[18528] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1326 gene, herein designated VGAM GENE, on one or more VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18529] It is yet further appreciated that a function of VGAM1326 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1326 correlate with, and may be deduced from, the identity of the host target genes which VGAM1326 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18530] Nucleotide sequences of the VGAM1326 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1326 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1326 are further described hereinbelow with reference to Table 1.

[18531] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1326 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18532] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1327 (VGAM1327) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18533] VGAM1327 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1327 was detected is described hereinabove with reference to Figs. 2-8.

[18534] VGAM1327 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 8. VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18535] VGAM1327 gene, herein designated VGAM GENE, encodes a VGAM1327 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1327 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1327 precursor RNA is designated SEQ ID:33895, and is provided hereinbelow with reference to the sequence listing part.

[18536] VGAM1327 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18537] An enzyme complex designated DICER COMPLEX, dices the VGAM1327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1327 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1327 RNA is designated SEQ ID:33896, and is provided hereinbelow with reference to the sequence listing part.

[18538] VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18539] VGAM1327 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1327 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1327 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18540] The complementary binding of VGAM1327 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1327 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1327 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18541] It is appreciated that VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1327 host target genes. The mRNA of each one of this plurality of VGAM1327 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1327 RNA, herein designated VGAM RNA, and which when bound by VGAM1327 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1327 host target proteins.

[18542] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1327 gene, herein designated VGAM GENE, on one or more VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18543] It is yet further appreciated that a function of VGAM1327 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1327 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1327 correlate with, and may be deduced from, the identity of the host target genes which VGAM1327 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18544] Nucleotide sequences of the VGAM1327 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1327 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1327 are further described hereinbelow with reference to Table 1.

[18545] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1327 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18546] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1328 (VGAM1328) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18547] VGAM1328 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1328 was detected is described hereinabove with reference to Figs. 2-8.

[18548] VGAM1328 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8.

VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18549] VGAM1328 gene, herein designated VGAM GENE, encodes a VGAM1328 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1328 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1328 precursor RNA is designated SEQ ID:33909, and is provided hereinbelow with reference to the sequence listing part.

[18550] VGAM1328 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18551] An enzyme complex designated DICER COMPLEX, dices

the VGAM1328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1328 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1328 RNA is designated SEQ ID:33910, and is provided hereinbelow with reference to the sequence listing part.

[18552] VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18553] VGAM1328 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1328 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1328 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18554] The complementary binding of VGAM1328 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1328 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18555] It is appreciated that VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1328 host target genes. The mRNA of each one of this plurality of VGAM1328 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1328 RNA, herein designated VGAM RNA, and which when bound by VGAM1328 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1328 host target proteins.

[18556] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1328 gene, herein designated VGAM GENE, on one or more VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18557] It is yet further appreciated that a function of VGAM1328 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1328 correlate with, and may be deduced from, the identity of the host target genes which VGAM1328 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18558] Nucleotide sequences of the VGAM1328 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1328 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1328 are further described hereinbelow with reference to Table 1.

[18559] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1328 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18560] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1329 (VGAM1329) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18561] VGAM1329 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1329 was detected is described hereinabove with reference to Figs. 2-8.

[18562] VGAM1329 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM1329 host target gene, herein designated VGAM



HOST TARGET GENE, is a human gene contained in the human genome.

[18563] VGAM1329 gene, herein designated VGAM GENE, encodes a VGAM1329 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1329 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1329 precursor RNA is designated SEQ ID:33928, and is provided hereinbelow with reference to the sequence listing part.

[18564] VGAM1329 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18565] An enzyme complex designated DICER COMPLEX, dices the VGAM1329 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1329 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1329 RNA is designated SEQ ID:33929, and is provided hereinbelow with reference to the sequence listing part.

[18566] VGAM1329 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18567] VGAM1329 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1329 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18568] The complementary binding of VGAM1329 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1329

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1329 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18569] It is appreciated that VGAM1329 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1329 host target genes. The mRNA of each one of this plurality of VGAM1329 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1329 RNA, herein designated VGAM RNA, and which when bound by VGAM1329 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1329 host target proteins.

[18570] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1329 gene, herein designated VGAM GENE, on one or more VGAM1329 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18571] It is yet further appreciated that a function of VGAM1329 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1329 correlate with, and may be deduced from, the identity of the host target genes which VGAM1329 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18572] Nucleotide sequences of the VGAM1329 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1329 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1329 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1329 are further described hereinbelow with reference to Table 1.

[18573] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1329 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18574] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1330 (VGAM1330) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18575] VGAM1330 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1330 was detected is described hereinabove with reference to Figs. 2-8.

[18576] VGAM1330 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[18577] VGAM1330 gene, herein designated VGAM GENE, encodes a VGAM1330 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1330 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1330 precursor RNA is designated SEQ ID:33940, and is provided hereinbelow with reference to the sequence listing part.

[18578] VGAM1330 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18579] An enzyme complex designated DICER COMPLEX, dices the VGAM1330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1330 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1330 RNA is designated SEQ ID:33941, and is provided hereinbelow with reference to the sequence listing part.

[18580] VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18581] VGAM1330 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1330 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18582] The complementary binding of VGAM1330 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1330 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1330 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18583] It is appreciated that VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1330 host target genes. The mRNA of each one of this plurality of VGAM1330 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1330 RNA, herein designated VGAM RNA, and which when bound by VGAM1330 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1330 host target proteins.

[18584] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1330 gene, herein designated VGAM GENE, on one or more VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18585] It is yet further appreciated that a function of VGAM1330 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1330 correlate with, and may be deduced from, the identity of the host target genes which VGAM1330 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18586] Nucleotide sequences of the VGAM1330 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1330 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1330 are further

described hereinbelow with reference to Table 1.

[18587] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1330 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18588] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1331 (VGAM1331) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18589] VGAM1331 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1331 was detected is described hereinabove with reference to Figs. 2-8.

[18590] VGAM1331 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18591] VGAM1331 gene, herein designated VGAM GENE, encodes a VGAM1331 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1331 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1331 precursor RNA is designated SEQ ID:33945, and is provided hereinbelow with reference to the sequence listing part.

[18592] VGAM1331 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18593] An enzyme complex designated DICER COMPLEX, dices the VGAM1331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1331 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1331 RNA is designated SEQ ID:33946, and is provided hereinbelow with reference to the sequence listing part.

[18594] VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18595] VGAM1331 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1331 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1331 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18596] The complementary binding of VGAM1331 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1331 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18597] It is appreciated that VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1331 host target genes. The mRNA of each one of this plurality of VGAM1331 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1331 RNA, herein designated VGAM RNA, and which when bound by VGAM1331 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1331 host target proteins.

[18598] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1331 gene, herein designated VGAM GENE, on one or more VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18599] It is yet further appreciated that a function of VGAM1331 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1331 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1331 correlate with, and may be deduced from, the identity of the host target genes which VGAM1331 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18600] Nucleotide sequences of the VGAM1331 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1331 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1331 are further described hereinbelow with reference to Table 1.

[18601] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1331 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18602] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1332 (VGAM1332) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18603] VGAM1332 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1332 was detected is described hereinabove with reference to Figs. 2-8.

[18604] VGAM1332 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1332 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18605] VGAM1332 gene, herein designated VGAM GENE, encodes

a VGAM1332 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1332 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1332 precursor RNA is designated SEQ ID:33952, and is provided hereinbelow with reference to the sequence listing part.

[18606] VGAM1332 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18607] An enzyme complex designated DICER COMPLEX, dices the VGAM1332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1332 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1332 RNA is designated SEQ ID:33953, and is provided hereinbelow with reference to the sequence listing part.

[18608] VGAM1332 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18609] VGAM1332 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1332 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18610] The complementary binding of VGAM1332 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1332 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[18611] It is appreciated that VGAM1332 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1332 host target genes. The mRNA of each one of this plurality of VGAM1332 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1332 RNA, herein designated VGAM RNA, and which when bound by VGAM1332 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1332 host target proteins.

[18612] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1332 gene, herein designated VGAM GENE, on one or more VGAM1332 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18613] It is yet further appreciated that a function of VGAM1332 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1332 correlate with, and may be deduced from, the identity of the host target genes which VGAM1332 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18614] Nucleotide sequences of the VGAM1332 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1332 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1332 are further described hereinbelow with reference to Table 1.

[18615] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1332 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18616] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1333 (VGAM1333) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18617] VGAM1333 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1333 was detected is described hereinabove with reference to Figs. 2-8.

[18618] VGAM1333 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18619] VGAM1333 gene, herein designated VGAM GENE, encodes a VGAM1333 precursor RNA, herein designated VGAM



PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1333 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1333 precursor RNA is designated SEQ ID:33958, and is provided hereinbelow with reference to the sequence listing part.

[18620] VGAM1333 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18621] An enzyme complex designated DICER COMPLEX, dices the VGAM1333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1333 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1333 RNA is designated SEQ ID:33959, and is provided hereinbelow with reference to the sequence listing part.

[18622] VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18623] VGAM1333 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1333 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18624] The complementary binding of VGAM1333 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1333 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18625] It is appreciated that VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1333 host target genes. The mRNA of each one of this plurality of VGAM1333 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1333 RNA, herein designated VGAM RNA, and which when bound by VGAM1333 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1333 host target proteins.

[18626] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1333 gene, herein designated VGAM GENE, on one or more VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18627] It is yet further appreciated that a function of VGAM1333 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1333 correlate with, and may be deduced from, the identity of the host target genes which VGAM1333 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18628] Nucleotide sequences of the VGAM1333 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1333 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1333 are further described hereinbelow with reference to Table 1.

[18629] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1333 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18630] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1334 (VGAM1334) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18631] VGAM1334 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1334 was detected is described hereinabove with reference to Figs. 2-8.

[18632] VGAM1334 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1334 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18633] VGAM1334 gene, herein designated VGAM GENE, encodes a VGAM1334 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1334 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1334 precursor RNA is designated SEQ ID:33964, and is provided hereinbelow with reference to the sequence listing part.

[18634] VGAM1334 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18635] An enzyme complex designated DICER COMPLEX, dices the VGAM1334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1334 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1334 RNA is designated SEQ ID:33965, and is provided hereinbelow with reference to the sequence listing part.

[18636] VGAM1334 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18637] VGAM1334 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1334 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1334 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18638] The complementary binding of VGAM1334 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1334 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18639] It is appreciated that VGAM1334 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1334 host target genes. The mRNA of each one of this plurality of VGAM1334 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1334 RNA, herein designated VGAM RNA, and which when bound by VGAM1334 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1334 host target proteins.

[18640] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1334 gene, herein designated VGAM GENE, on one or more VGAM1334 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18641] It is yet further appreciated that a function of VGAM1334 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1334 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1334 correlate with, and may be deduced from, the identity of the host target genes which VGAM1334 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18642] Nucleotide sequences of the VGAM1334 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1334 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1334 are further described hereinbelow with reference to Table 1.

[18643] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1334 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18644] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1335 (VGAM1335) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18645] VGAM1335 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1335 was detected is described hereinabove with reference to Figs. 2–8.

[18646] VGAM1335 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Feline leukemia virus. VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18647] VGAM1335 gene, herein designated VGAM GENE, encodes a VGAM1335 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1335 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1335 precursor RNA is designated SEQ ID:33969, and is provided hereinbelow with reference to the sequence listing part.

[18648] VGAM1335 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18649] An enzyme complex designated DICER COMPLEX, dices the VGAM1335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1335 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1335 RNA is designated SEQ ID:33970, and is provided hereinbelow with reference to the sequence listing part.

[18650] VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18651] VGAM1335 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1335 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18652] The complementary binding of VGAM1335 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1335 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18653] It is appreciated that VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1335 host target genes. The mRNA of each one of this plurality of VGAM1335 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1335 RNA, herein designated VGAM RNA, and which when bound by VGAM1335 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1335 host target proteins.

[18654] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1335 gene, herein designated VGAM GENE, on one or more VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [18655] It is yet further appreciated that a function of VGAM1335 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of viral infection by Feline leukemia virus. Specific functions, and accordingly utilities, of VGAM1335 correlate with, and may be deduced from, the identity of the host target genes which VGAM1335 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [18656] Nucleotide sequences of the VGAM1335 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1335 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1335 are further described hereinbelow with reference to Table 1.
- [18657] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1335 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18658] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1336 (VGAM1336) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18659] VGAM1336 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1336 was detected is described hereinabove with reference to Figs. 2–8.

[18660] VGAM1336 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18661] VGAM1336 gene, herein designated VGAM GENE, encodes a VGAM1336 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1336 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1336 precursor RNA is designated SEQ ID:34001, and is provided hereinbelow with reference to the sequence listing part.

[18662] VGAM1336 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18663] An enzyme complex designated DICER COMPLEX, dices the VGAM1336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1336 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1336 RNA is designated SEQ ID:34002, and is provided hereinbelow with reference to the sequence listing part.

[18664] VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18665] VGAM1336 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1336 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1336 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18666] The complementary binding of VGAM1336 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1336 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18667] It is appreciated that VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1336 host target genes. The mRNA of

each one of this plurality of VGAM1336 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1336 RNA, herein designated VGAM RNA, and which when bound by VGAM1336 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1336 host target proteins.

[18668] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1336 gene, herein designated VGAM GENE, on one or more VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[18669] It is yet further appreciated that a function of VGAM1336 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1336 correlate with, and may be deduced from, the identity of the host target genes which VGAM1336 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18670] Nucleotide sequences of the VGAM1336 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1336 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1336 are further described hereinbelow with reference to Table 1.

[18671] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1336 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[18672] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1337 (VGAM1337) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18673] VGAM1337 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1337 was detected is described hereinabove with reference to Figs. 2–8.

[18674] VGAM1337 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus A. VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18675] VGAM1337 gene, herein designated VGAM GENE, encodes a VGAM1337 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1337 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly



similar to the nucleotide sequence of VGAM1337 precursor RNA is designated SEQ ID:34006, and is provided hereinbelow with reference to the sequence listing part.

[18676] VGAM1337 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18677] An enzyme complex designated DICER COMPLEX, dices the VGAM1337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1337 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1337 RNA is designated SEQ ID:34007,

and is provided hereinbelow with reference to the sequence listing part.

[18678] VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18679] VGAM1337 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1337 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1337 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18680] The complementary binding of VGAM1337 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1337 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18681] It is appreciated that VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1337 host target genes. The mRNA of each one of this plurality of VGAM1337 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1337 RNA, herein designated VGAM RNA, and which when bound by VGAM1337 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1337 host target proteins.

[18682] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1337 gene, herein designated VGAM GENE, on one or more VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18683] It is yet further appreciated that a function of VGAM1337 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1337 include diagnosis, prevention and treatment of viral infection by Human adenovirus A. Specific functions, and accordingly utilities, of VGAM1337 correlate with, and may be deduced from, the identity of the host target genes which VGAM1337 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18684] Nucleotide sequences of the VGAM1337 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1337 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1337 are further described hereinbelow with reference to Table 1.

[18685] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1337 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18686] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1338 (VGAM1338) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18687] VGAM1338 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1338 was detected is described hereinabove with reference to Figs. 2–8.

[18688] VGAM1338 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid herpesvirus 1. VGAM1338 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18689] VGAM1338 gene, herein designated VGAM GENE, encodes a VGAM1338 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1338 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1338 precu-

sor RNA is designated SEQ ID:34163, and is provided hereinbelow with reference to the sequence listing part.

[18690] VGAM1338 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18691] An enzyme complex designated DICER COMPLEX, dices the VGAM1338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1338 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1338 RNA is designated SEQ ID:34164, and is provided hereinbelow with reference to the se-

quence listing part.

[18692] VGAM1338 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18693] VGAM1338 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1338 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM1338 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18694] The complementary binding of VGAM1338 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1338 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18695] It is appreciated that VGAM1338 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1338 host target genes. The mRNA of each one of this plurality of VGAM1338 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1338 RNA, herein designated VGAM RNA, and which when bound by VGAM1338 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1338 host target proteins.

[18696] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1338 gene, herein designated VGAM GENE, on one or more VGAM1338 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18697] It is yet further appreciated that a function of VGAM1338

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1338 include diagnosis, prevention and treatment of viral infection by Meleagrid herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1338 correlate with, and may be deduced from, the identity of the host target genes which VGAM1338 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18698] Nucleotide sequences of the VGAM1338 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1338 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1338 are further described hereinbelow with reference to Table 1.

[18699] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1338 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18700] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1339 (VGAM1339) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18701] VGAM1339 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1339 was detected is described hereinabove with reference to Figs. 2–8.

[18702] VGAM1339 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus A. VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18703] VGAM1339 gene, herein designated VGAM GENE, encodes a VGAM1339 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1339 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1339 precursor RNA is designated SEQ ID:34166, and is provided

hereinbelow with reference to the sequence listing part.

[18704] VGAM1339 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18705] An enzyme complex designated DICER COMPLEX, dices the VGAM1339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1339 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1339 RNA is designated SEQ ID:34167, and is provided hereinbelow with reference to the sequence listing part.

[18706] VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18707] VGAM1339 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1339 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1339 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18708] The complementary binding of VGAM1339 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1339 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18709] It is appreciated that VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1339 host target genes. The mRNA of each one of this plurality of VGAM1339 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1339 RNA, herein designated VGAM RNA, and which when bound by VGAM1339 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1339 host target proteins.

[18710] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1339 gene, herein designated VGAM GENE, on one or more VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18711] It is yet further appreciated that a function of VGAM1339 is inhibition of expression of host target genes, as part of



a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1339 include diagnosis, prevention and treatment of viral infection by Human adenovirus A. Specific functions, and accordingly utilities, of VGAM1339 correlate with, and may be deduced from, the identity of the host target genes which VGAM1339 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18712] Nucleotide sequences of the VGAM1339 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1339 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1339 are further described hereinbelow with reference to Table 1.

[18713] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1339 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18714] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1340 (VGAM1340) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18715] VGAM1340 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1340 was detected is described hereinabove with reference to Figs. 2–8.

[18716] VGAM1340 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1340 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18717] VGAM1340 gene, herein designated VGAM GENE, encodes a VGAM1340 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1340 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1340 precursor RNA is designated SEQ ID:34171, and is provided hereinbelow with reference to the sequence listing part.

[18718] VGAM1340 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18719] An enzyme complex designated DICER COMPLEX, dices the VGAM1340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1340 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1340 RNA is designated SEQ ID:34172, and is provided hereinbelow with reference to the sequence listing part.

[18720] VGAM1340 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18721] VGAM1340 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1340 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18722] The complementary binding of VGAM1340 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1340 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18723] It is appreciated that VGAM1340 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1340 host target genes. The mRNA of each one of this plurality of VGAM1340 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1340 RNA, herein designated VGAM

RNA, and which when bound by VGAM1340 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1340 host target proteins.

[18724] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1340 gene, herein designated VGAM GENE, on one or more VGAM1340 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18725] It is yet further appreciated that a function of VGAM1340 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1340 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1340 correlate with, and may be deduced from, the identity of the host target genes which VGAM1340 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18726] Nucleotide sequences of the VGAM1340 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1340 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1340 are further described hereinbelow with reference to Table 1.

[18727] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1340 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18728] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1341 (VGAM1341) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18729] VGAM1341 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1341 was detected is described hereinabove with reference to Figs. 2–8.

[18730] VGAM1341 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18731] VGAM1341 gene, herein designated VGAM GENE, encodes a VGAM1341 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1341 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1341 precursor RNA is designated SEQ ID:34183, and is provided hereinbelow with reference to the sequence listing part.

[18732] VGAM1341 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM1341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18733] An enzyme complex designated DICER COMPLEX, dices the VGAM1341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1341 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1341 RNA is designated SEQ ID:34184, and is provided hereinbelow with reference to the sequence listing part.

[18734] VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18735] VGAM1341 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1341 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1341 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1341 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18736] The complementary binding of VGAM1341 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1341 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18737] It is appreciated that VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1341 host target genes. The mRNA of each one of this plurality of VGAM1341 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1341 RNA, herein designated VGAM RNA, and which when bound by VGAM1341 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1341 host target proteins.

[18738] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1341 gene, herein designated VGAM GENE, on one or more VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18739] It is yet further appreciated that a function of VGAM1341 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1341 include diagnosis, prevention and

treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1341 correlate with, and may be deduced from, the identity of the host target genes which VGAM1341 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18740] Nucleotide sequences of the VGAM1341 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1341 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1341 are further described hereinbelow with reference to Table 1.

[18741] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1341 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18742] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1342 (VGAM1342) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18743] VGAM1342 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1342 was detected is described hereinabove with reference to Figs. 2–8.

[18744] VGAM1342 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18745] VGAM1342 gene, herein designated VGAM GENE, encodes a VGAM1342 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1342 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1342 precursor RNA is designated SEQ ID:34224, and is provided hereinbelow with reference to the sequence listing part.

[18746] VGAM1342 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1342 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18747] An enzyme complex designated DICER COMPLEX, dices the VGAM1342 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1342 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1342 RNA is designated SEQ ID:34225, and is provided hereinbelow with reference to the sequence listing part.

[18748] VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1342 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18749] VGAM1342 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1342 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18750] The complementary binding of VGAM1342 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1342 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18751] It is appreciated that VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1342 host target genes. The mRNA of each one of this plurality of VGAM1342 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1342 RNA, herein designated VGAM RNA, and which when bound by VGAM1342 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1342 host target proteins.

[18752] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1342 gene, herein designated VGAM GENE, on one or more VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18753] It is yet further appreciated that a function of VGAM1342 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific

functions, and accordingly utilities, of VGAM1342 correlate with, and may be deduced from, the identity of the host target genes which VGAM1342 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18754] Nucleotide sequences of the VGAM1342 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1342 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1342 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1342 are further described hereinbelow with reference to Table 1.

[18755] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1342 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18756] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1343 (VGAM1343) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[18757] VGAM1343 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1343 was detected is described hereinabove with reference to Figs. 2–8.

[18758] VGAM1343 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM1343 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18759] VGAM1343 gene, herein designated VGAM GENE, encodes a VGAM1343 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1343 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1343 precursor RNA is designated SEQ ID:34230, and is provided hereinbelow with reference to the sequence listing part.

[18760] VGAM1343 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1343 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18761] An enzyme complex designated DICER COMPLEX, dices the VGAM1343 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1343 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1343 RNA is designated SEQ ID:34231, and is provided hereinbelow with reference to the sequence listing part.

[18762] VGAM1343 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1343 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18763] VGAM1343 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1343 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1343 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18764] The complementary binding of VGAM1343 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1343 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18765] It is appreciated that VGAM1343 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1343 host target genes. The mRNA of each one of this plurality of VGAM1343 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1343 RNA, herein designated VGAM RNA, and which when bound by VGAM1343 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1343 host target proteins.

[18766] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1343 gene, herein designated VGAM GENE, on one or more VGAM1343 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18767] It is yet further appreciated that a function of VGAM1343 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1343 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1343



correlate with, and may be deduced from, the identity of the host target genes which VGAM1343 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18768] Nucleotide sequences of the VGAM1343 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1343 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1343 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1343 are further described hereinbelow with reference to Table 1.

[18769] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1343 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18770] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1344 (VGAM1344) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[18771] VGAM1344 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1344 was detected is described hereinabove with reference to Figs. 2–8.

[18772] VGAM1344 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 4. VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18773] VGAM1344 gene, herein designated VGAM GENE, encodes a VGAM1344 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1344 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1344 precursor RNA is designated SEQ ID:34272, and is provided hereinbelow with reference to the sequence listing part.

[18774] VGAM1344 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18775] An enzyme complex designated DICER COMPLEX, dices the VGAM1344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1344 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1344 RNA is designated SEQ ID:34273, and is provided hereinbelow with reference to the sequence listing part.

[18776] VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18777] VGAM1344 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1344 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1344 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18778] The complementary binding of VGAM1344 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1344 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18779] It is appreciated that VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1344 host target genes. The mRNA of each one of this plurality of VGAM1344 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1344 RNA, herein designated VGAM RNA, and which when bound by VGAM1344 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1344 host target proteins.

[18780] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1344 gene, herein designated VGAM GENE, on one or more VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18781] It is yet further appreciated that a function of VGAM1344 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1344 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1344 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1344 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18782] Nucleotide sequences of the VGAM1344 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1344 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1344 are further described hereinbelow with reference to Table 1.

[18783] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1344 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18784] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1345 (VGAM1345) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18785] VGAM1345 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1345 was detected is described hereinabove with reference to Figs. 2-8.

[18786] VGAM1345 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18787] VGAM1345 gene, herein designated VGAM GENE, encodes a VGAM1345 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1345 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1345 precursor RNA is designated SEQ ID:34284, and is provided hereinbelow with reference to the sequence listing part.

[18788] VGAM1345 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18789] An enzyme complex designated DICER COMPLEX, dices the VGAM1345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1345 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1345 RNA is designated SEQ ID:34285, and is provided hereinbelow with reference to the sequence listing part.

[18790] VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18791] VGAM1345 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1345 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18792] The complementary binding of VGAM1345 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1345 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18793] It is appreciated that VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1345 host target genes. The mRNA of each one of this plurality of VGAM1345 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1345 RNA, herein designated VGAM RNA, and which when bound by VGAM1345 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1345 host target proteins.

[18794] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1345 gene, herein designated VGAM GENE, on one or more VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18795] It is yet further appreciated that a function of VGAM1345 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1345 correlate with, and may be deduced from, the identity of the host target genes which VGAM1345 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[18796] Nucleotide sequences of the VGAM1345 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1345 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1345 are further described hereinbelow with reference to Table 1.

[18797] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1345 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18798] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1346 (VGAM1346) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18799] VGAM1346 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1346 was detected is described hereinabove with reference to Figs. 2–8.

[18800] VGAM1346 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8. VGAM1346 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18801] VGAM1346 gene, herein designated VGAM GENE, encodes a VGAM1346 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1346 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1346 precursor RNA is designated SEQ ID:34290, and is provided hereinbelow with reference to the sequence listing part.

[18802] VGAM1346 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18803] An enzyme complex designated DICER COMPLEX, dices the VGAM1346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1346 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1346 RNA is designated SEQ ID:34291, and is provided hereinbelow with reference to the sequence listing part.

[18804] VGAM1346 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18805] VGAM1346 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1346 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1346 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[18806] The complementary binding of VGAM1346 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1346 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18807] It is appreciated that VGAM1346 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1346 host target genes. The mRNA of each one of this plurality of VGAM1346 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1346 RNA, herein designated VGAM RNA, and which when bound by VGAM1346 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1346 host target proteins.

[18808] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1346 gene, herein designated VGAM GENE, on one or more VGAM1346 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18809] It is yet further appreciated that a function of VGAM1346 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1346 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1346 correlate with, and may be deduced from, the identity of the host target genes which VGAM1346 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[18810] Nucleotide sequences of the VGAM1346 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1346 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1346 are further described hereinbelow with reference to Table 1.

[18811] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1346 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18812] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1347 (VGAM1347) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18813] VGAM1347 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1347 was detected is described hereinabove with reference to Figs. 2–8.

[18814] VGAM1347 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18815] VGAM1347 gene, herein designated VGAM GENE, encodes a VGAM1347 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1347 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1347 precursor RNA is designated SEQ ID:34317, and is provided hereinbelow with reference to the sequence listing part.

[18816] VGAM1347 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1347 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18817] An enzyme complex designated DICER COMPLEX, dices the VGAM1347 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1347 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 100%) nucleotide sequence of VGAM1347 RNA is designated SEQ ID:34318, and is provided hereinbelow with reference to the sequence listing part.

[18818] VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[18819] VGAM1347 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1347 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1347 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18820] The complementary binding of VGAM1347 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1347 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18821] It is appreciated that VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1347 host target genes. The mRNA of each one of this plurality of VGAM1347 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1347 RNA, herein designated VGAM RNA, and which when bound by VGAM1347 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1347 host target proteins.

[18822] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1347 gene, herein designated VGAM GENE, on one

or more VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18823] It is yet further appreciated that a function of VGAM1347 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1347 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1347 correlate with, and may be deduced from, the identity of the host target genes which VGAM1347 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[18824] Nucleotide sequences of the VGAM1347 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1347 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1347 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1347 are further described hereinbelow with reference to Table 1.

[18825] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1347 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18826] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1348 (VGAM1348) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18827] VGAM1348 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1348 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[18828] VGAM1348 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 8.

VGAM1348 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18829] VGAM1348 gene, herein designated VGAM GENE, encodes a VGAM1348 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1348 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1348 precursor RNA is designated SEQ ID:34332, and is provided hereinbelow with reference to the sequence listing part.

[18830] VGAM1348 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1348 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18831] An enzyme complex designated DICER COMPLEX, dices the VGAM1348 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1348 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1348 RNA is designated SEQ ID:34333, and is provided hereinbelow with reference to the sequence listing part.

[18832] VGAM1348 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18833] VGAM1348 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1348 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18834] The complementary binding of VGAM1348 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1348 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18835] It is appreciated that VGAM1348 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1348 host target genes. The mRNA of each one of this plurality of VGAM1348 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1348 RNA, herein designated VGAM RNA, and which when bound by VGAM1348 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1348 host target proteins.

[18836] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1348 gene, herein designated VGAM GENE, on one or more VGAM1348 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18837] It is yet further appreciated that a function of VGAM1348 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1348 correlate with, and may be deduced from, the identity of the host target genes which VGAM1348 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18838] Nucleotide sequences of the VGAM1348 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the duced VGAM1348 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1348 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1348 are further described hereinbelow with reference to Table 1.

[18839] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1348 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18840] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1349 (VGAM1349) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18841] VGAM1349 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1349 was detected is described hereinabove with reference to Figs. 2-8.

[18842] VGAM1349 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus.

VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18843] VGAM1349 gene, herein designated VGAM GENE, encodes a VGAM1349 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1349 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1349 precursor RNA is designated SEQ ID:34359, and is provided hereinbelow with reference to the sequence listing part.

[18844] VGAM1349 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[18845] An enzyme complex designated DICER COMPLEX, dices the VGAM1349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1349 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1349 RNA is designated SEQ ID:34360, and is provided hereinbelow with reference to the sequence listing part.

[18846] VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18847] VGAM1349 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1349 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1349 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18848] The complementary binding of VGAM1349 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1349 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18849] It is appreciated that VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1349 host target genes. The mRNA of each one of this plurality of VGAM1349 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1349 RNA, herein designated VGAM RNA, and which when bound by VGAM1349 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1349 host target proteins.

[18850] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1349 gene, herein designated VGAM GENE, on one or more VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18851] It is yet further appreciated that a function of VGAM1349 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1349 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1349 correlate with, and may be deduced from, the identity of the host target genes which VGAM1349 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18852] Nucleotide sequences of the VGAM1349 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1349 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1349 are further described hereinbelow with reference to Table 1.

[18853] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1349 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18854] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1350 (VGAM1350) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18855] VGAM1350 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1350 was detected is described hereinabove with reference to Figs. 2-8.

[18856] VGAM1350 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Ectromelia virus.

VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18857] VGAM1350 gene, herein designated VGAM GENE, encodes a VGAM1350 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1350 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1350 precursor RNA is designated SEQ ID:34365, and is provided hereinbelow with reference to the sequence listing part.

[18858] VGAM1350 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18859] An enzyme complex designated DICER COMPLEX, dices the VGAM1350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1350 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1350 RNA is designated SEQ ID:34366, and is provided hereinbelow with reference to the sequence listing part.

[18860] VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18861] VGAM1350 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1350 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1350 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18862] The complementary binding of VGAM1350 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1350 host target RNA, herein designated VGAM



HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1350 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18863] It is appreciated that VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1350 host target genes. The mRNA of each one of this plurality of VGAM1350 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1350 RNA, herein designated VGAM RNA, and which when bound by VGAM1350 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1350 host target proteins.

[18864] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1350 gene, herein designated VGAM GENE, on one or more VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18865] It is yet further appreciated that a function of VGAM1350 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1350 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1350 correlate with, and may be deduced from, the identity of the host target genes which VGAM1350 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18866] Nucleotide sequences of the VGAM1350 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1350 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1350 are further described hereinbelow with reference to Table 1.

[18867] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1350 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18868] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1351 (VGAM1351) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18869] VGAM1351 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1351 was detected is described hereinabove with reference to Figs. 2-8.

[18870] VGAM1351 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gibbon ape leukemia

virus. VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18871] VGAM1351 gene, herein designated VGAM GENE, encodes a VGAM1351 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1351 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1351 precursor RNA is designated SEQ ID:34369, and is provided hereinbelow with reference to the sequence listing part.

[18872] VGAM1351 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1351 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18873] An enzyme complex designated DICER COMPLEX, dices

the VGAM1351 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1351 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1351 RNA is designated SEQ ID:34370, and is provided hereinbelow with reference to the sequence listing part.

[18874] VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18875] VGAM1351 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1351 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1351 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1351 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18876] The complementary binding of VGAM1351 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1351 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18877] It is appreciated that VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1351 host target genes. The mRNA of each one of this plurality of VGAM1351 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1351 RNA, herein designated VGAM RNA, and which when bound by VGAM1351 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1351 host target proteins.

[18878] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1351 gene, herein designated VGAM GENE, on one or more VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18879] It is yet further appreciated that a function of VGAM1351 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1351 include diagnosis, prevention and treatment of viral infection by Gibbon ape leukemia virus. Specific functions, and accordingly utilities, of VGAM1351 correlate with, and may be deduced from, the identity of the host target genes which VGAM1351 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18880] Nucleotide sequences of the VGAM1351 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1351 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM1351 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1351 are further described hereinbelow with reference to Table 1.

[18881] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1351 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18882] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1352 (VGAM1352) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18883] VGAM1352 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1352 was detected is described hereinabove with reference to Figs. 2-8.

[18884] VGAM1352 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1352 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[18885] VGAM1352 gene, herein designated VGAM GENE, encodes a VGAM1352 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1352 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1352 precursor RNA is designated SEQ ID:34413, and is provided hereinbelow with reference to the sequence listing part.

[18886] VGAM1352 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1352 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18887] An enzyme complex designated DICER COMPLEX, dices the VGAM1352 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1352 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1352 RNA is designated SEQ ID:34414, and is provided hereinbelow with reference to the sequence listing part.

[18888] VGAM1352 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18889] VGAM1352 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1352 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1352 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18890] The complementary binding of VGAM1352 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1352

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1352 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18891] It is appreciated that VGAM1352 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1352 host target genes. The mRNA of each one of this plurality of VGAM1352 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1352 RNA, herein designated VGAM RNA, and which when bound by VGAM1352 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1352 host target proteins.

[18892] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1352 gene, herein designated VGAM GENE, on one or more VGAM1352 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18893] It is yet further appreciated that a function of VGAM1352 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1352 include diagnosis, prevention and treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1352 correlate with, and may be deduced from, the identity of the host target genes which VGAM1352 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18894] Nucleotide sequences of the VGAM1352 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1352 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1352 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1352 are further described hereinbelow with reference to Table 1.

[18895] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1352 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18896] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1353 (VGAM1353) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18897] VGAM1353 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1353 was detected is described hereinabove with reference to Figs. 2-8.

[18898] VGAM1353 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus C. VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[18899] VGAM1353 gene, herein designated VGAM GENE, encodes a VGAM1353 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1353 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1353 precursor RNA is designated SEQ ID:34423, and is provided hereinbelow with reference to the sequence listing part.

[18900] VGAM1353 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18901] An enzyme complex designated DICER COMPLEX, dices the VGAM1353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1353 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1353 RNA is designated SEQ ID:34424, and is provided hereinbelow with reference to the sequence listing part.

[18902] VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18903] VGAM1353 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1353 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18904] The complementary binding of VGAM1353 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1353 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1353 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18905] It is appreciated that VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1353 host target genes. The mRNA of each one of this plurality of VGAM1353 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1353 RNA, herein designated VGAM RNA, and which when bound by VGAM1353 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1353 host target proteins.

[18906] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1353 gene, herein designated VGAM GENE, on one or more VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18907] It is yet further appreciated that a function of VGAM1353 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus C. Specific functions, and accordingly utilities, of VGAM1353 correlate with, and may be deduced from, the identity of the host target genes which VGAM1353 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18908] Nucleotide sequences of the VGAM1353 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1353 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1353 are further

described hereinbelow with reference to Table 1.

[18909] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1353 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18910] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1354 (VGAM1354) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18911] VGAM1354 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1354 was detected is described hereinabove with reference to Figs. 2-8.

[18912] VGAM1354 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus C. VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18913] VGAM1354 gene, herein designated VGAM GENE, encodes a VGAM1354 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1354 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1354 precursor RNA is designated SEQ ID:34493, and is provided hereinbelow with reference to the sequence listing part.

[18914] VGAM1354 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18915] An enzyme complex designated DICER COMPLEX, dices the VGAM1354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1354 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1354 RNA is designated SEQ ID:34494, and is provided hereinbelow with reference to the sequence listing part.

[18916] VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18917] VGAM1354 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1354 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1354 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18918] The complementary binding of VGAM1354 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1354 host target protein, herein desig-



nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18919] It is appreciated that VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1354 host target genes. The mRNA of each one of this plurality of VGAM1354 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1354 RNA, herein designated VGAM RNA, and which when bound by VGAM1354 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1354 host target proteins.

[18920] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1354 gene, herein designated VGAM GENE, on one or more VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18921] It is yet further appreciated that a function of VGAM1354 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus C. Specific functions, and accordingly utilities, of VGAM1354 correlate with, and may be deduced from, the identity of the host target genes which VGAM1354 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18922] Nucleotide sequences of the VGAM1354 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1354 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1354 are further described hereinbelow with reference to Table 1.

[18923] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1354 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18924] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1355 (VGAM1355) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18925] VGAM1355 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1355 was detected is described hereinabove with reference to Figs. 2-8.

[18926] VGAM1355 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus C. VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18927] VGAM1355 gene, herein designated VGAM GENE, encodes

a VGAM1355 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1355 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1355 precursor RNA is designated SEQ ID:34509, and is provided hereinbelow with reference to the sequence listing part.

[18928] VGAM1355 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18929] An enzyme complex designated DICER COMPLEX, dices the VGAM1355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1355 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1355 RNA is designated SEQ ID:34510, and is provided hereinbelow with reference to the sequence listing part.

[18930] VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18931] VGAM1355 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1355 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18932] The complementary binding of VGAM1355 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1355 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[18933] It is appreciated that VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1355 host target genes. The mRNA of each one of this plurality of VGAM1355 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1355 RNA, herein designated VGAM RNA, and which when bound by VGAM1355 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1355 host target proteins.

[18934] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1355 gene, herein designated VGAM GENE, on one or more VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18935] It is yet further appreciated that a function of VGAM1355 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus C. Specific functions, and accordingly utilities, of VGAM1355 correlate with, and may be deduced from, the identity of the host target genes which VGAM1355 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18936] Nucleotide sequences of the VGAM1355 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1355 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1355 are further described hereinbelow with reference to Table 1.

[18937] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1355 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18938] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1356 (VGAM1356) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18939] VGAM1356 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1356 was detected is described hereinabove with reference to Figs. 2-8.

[18940] VGAM1356 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus C. VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18941] VGAM1356 gene, herein designated VGAM GENE, encodes a VGAM1356 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1356 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1356 precursor RNA is designated SEQ ID:34522, and is provided hereinbelow with reference to the sequence listing part.

[18942] VGAM1356 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1356 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18943] An enzyme complex designated DICER COMPLEX, dices the VGAM1356 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1356 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1356 RNA is designated SEQ ID:34523, and is provided hereinbelow with reference to the sequence listing part.

[18944] VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18945] VGAM1356 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1356 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1356 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18946] The complementary binding of VGAM1356 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1356 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18947] It is appreciated that VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1356 host target genes. The mRNA of each one of this plurality of VGAM1356 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1356 RNA, herein designated VGAM RNA, and which when bound by VGAM1356 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1356 host target proteins.

[18948] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1356 gene, herein designated VGAM GENE, on one or more VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18949] It is yet further appreciated that a function of VGAM1356 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1356 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus C. Specific functions, and accordingly utilities, of VGAM1356 correlate with, and may be deduced from, the identity of the host target genes which VGAM1356 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18950] Nucleotide sequences of the VGAM1356 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1356 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1356 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1356 are further described hereinbelow with reference to Table 1.

[18951] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1356 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18952] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1357 (VGAM1357) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18953] VGAM1357 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1357 was detected is described hereinabove with reference to Figs. 2-8.

[18954] VGAM1357 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine adenovirus C. VGAM1357 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18955] VGAM1357 gene, herein designated VGAM GENE, encodes a VGAM1357 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1357 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1357 precursor RNA is designated SEQ ID:34530, and is provided hereinbelow with reference to the sequence listing part.

[18956] VGAM1357 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1357 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18957] An enzyme complex designated DICER COMPLEX, dices the VGAM1357 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1357 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1357 RNA is designated SEQ ID:34531, and is provided hereinbelow with reference to the sequence listing part.

[18958] VGAM1357 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18959] VGAM1357 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1357 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18960] The complementary binding of VGAM1357 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1357 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18961] It is appreciated that VGAM1357 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1357 host target genes. The mRNA of each one of this plurality of VGAM1357 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1357 RNA, herein designated VGAM RNA, and which when bound by VGAM1357 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1357 host target proteins.

[18962] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1357 gene, herein designated VGAM GENE, on one or more VGAM1357 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[18963] It is yet further appreciated that a function of VGAM1357 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of viral infection by Porcine adenovirus C. Specific functions, and accordingly utilities, of VGAM1357 correlate with, and may be deduced from, the identity of the host target genes which VGAM1357 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18964] Nucleotide sequences of the VGAM1357 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1357 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1357 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1357 are further described hereinbelow with reference to Table 1.

[18965] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1357 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18966] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1358 (VGAM1358) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18967] VGAM1358 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1358 was detected is described hereinabove with reference to Figs. 2–8.

[18968] VGAM1358 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18969] VGAM1358 gene, herein designated VGAM GENE, encodes a VGAM1358 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1358 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1358 precursor RNA is designated SEQ ID:34546, and is provided hereinbelow with reference to the sequence listing part.

[18970] VGAM1358 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18971] An enzyme complex designated DICER COMPLEX, dices the VGAM1358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1358 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1358 RNA is designated SEQ ID:34547, and is provided hereinbelow with reference to the sequence listing part.

[18972] VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18973] VGAM1358 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1358 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1358 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18974] The complementary binding of VGAM1358 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1358 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18975] It is appreciated that VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1358 host target genes. The mRNA of each one of this plurality of VGAM1358 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1358 RNA, herein designated VGAM RNA, and which when bound by VGAM1358 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1358 host target proteins.

[18976] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1358 gene, herein designated VGAM GENE, on one or more VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [18977] It is yet further appreciated that a function of VGAM1358 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1358 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM1358 correlate with, and may be deduced from, the identity of the host target genes which VGAM1358 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [18978] Nucleotide sequences of the VGAM1358 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1358 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1358 are further described hereinbelow with reference to Table 1.
- [18979] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1358 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[18980] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1359 (VGAM1359) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18981] VGAM1359 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1359 was detected is described hereinabove with reference to Figs. 2-8.

[18982] VGAM1359 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit fibroma virus. VGAM1359 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18983] VGAM1359 gene, herein designated VGAM GENE, encodes a VGAM1359 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1359 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1359 precursor RNA is designated SEQ ID:34563, and is provided hereinbelow with reference to the sequence listing part.

[18984] VGAM1359 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1359 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18985] An enzyme complex designated DICER COMPLEX, dices the VGAM1359 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1359 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1359 RNA is designated SEQ ID:34564, and is provided hereinbelow with reference to the sequence listing part.

[18986] VGAM1359 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[18987] VGAM1359 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1359 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[18988] The complementary binding of VGAM1359 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1359 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[18989] It is appreciated that VGAM1359 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1359 host target genes. The mRNA of

each one of this plurality of VGAM1359 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1359 RNA, herein designated VGAM RNA, and which when bound by VGAM1359 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1359 host target proteins.

[18990] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1359 gene, herein designated VGAM GENE, on one or more VGAM1359 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[18991] It is yet further appreciated that a function of VGAM1359 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of viral infection by Rabbit fibroma virus. Specific functions, and accordingly utilities, of VGAM1359 correlate with, and may be deduced from, the identity of the host target genes which VGAM1359 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[18992] Nucleotide sequences of the VGAM1359 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1359 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1359 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1359 are further described hereinbelow with reference to Table 1.

[18993] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1359 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[18994] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1360 (VGAM1360) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[18995] VGAM1360 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1360 was detected is described hereinabove with reference to Figs. 2–8.

[18996] VGAM1360 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[18997] VGAM1360 gene, herein designated VGAM GENE, encodes a VGAM1360 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1360 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1360 precursor RNA is designated SEQ ID:34572, and is provided hereinbelow with reference to the sequence listing part.

[18998] VGAM1360 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[18999] An enzyme complex designated DICER COMPLEX, dices the VGAM1360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1360 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1360 RNA is designated SEQ ID:34573,

and is provided hereinbelow with reference to the sequence listing part.

[19000] VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19001] VGAM1360 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1360 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1360 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19002] The complementary binding of VGAM1360 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1360 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19003] It is appreciated that VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1360 host target genes. The mRNA of each one of this plurality of VGAM1360 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1360 RNA, herein designated VGAM RNA, and which when bound by VGAM1360 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1360 host target proteins.

[19004] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1360 gene, herein designated VGAM GENE, on one or more VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19005] It is yet further appreciated that a function of VGAM1360 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1360 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1360 correlate with, and may be deduced from, the identity of the host target genes which VGAM1360 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19006] Nucleotide sequences of the VGAM1360 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1360 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1360 are further described hereinbelow with reference to Table 1.

[19007] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1360 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19008] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1361 (VGAM1361) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19009] VGAM1361 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1361 was detected is described hereinabove with reference to Figs. 2–8.

[19010] VGAM1361 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19011] VGAM1361 gene, herein designated VGAM GENE, encodes a VGAM1361 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1361 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1361 precu-

sor RNA is designated SEQ ID:34749, and is provided hereinbelow with reference to the sequence listing part.

[19012] VGAM1361 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19013] An enzyme complex designated DICER COMPLEX, dices the VGAM1361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1361 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1361 RNA is designated SEQ ID:34750, and is provided hereinbelow with reference to the se-



quence listing part.

[19014] VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19015] VGAM1361 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1361 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19016] The complementary binding of VGAM1361 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1361 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19017] It is appreciated that VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1361 host target genes. The mRNA of each one of this plurality of VGAM1361 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1361 RNA, herein designated VGAM RNA, and which when bound by VGAM1361 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1361 host target proteins.

[19018] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1361 gene, herein designated VGAM GENE, on one or more VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19019] It is yet further appreciated that a function of VGAM1361

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1361 correlate with, and may be deduced from, the identity of the host target genes which VGAM1361 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19020] Nucleotide sequences of the VGAM1361 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1361 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1361 are further described hereinbelow with reference to Table 1.

[19021] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1361 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19022] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1362 (VGAM1362) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19023] VGAM1362 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1362 was detected is described hereinabove with reference to Figs. 2–8.

[19024] VGAM1362 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19025] VGAM1362 gene, herein designated VGAM GENE, encodes a VGAM1362 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1362 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1362 precursor RNA is designated SEQ ID:34779, and is provided

hereinbelow with reference to the sequence listing part.

[19026] VGAM1362 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19027] An enzyme complex designated DICER COMPLEX, dices the VGAM1362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1362 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1362 RNA is designated SEQ ID:34780, and is provided hereinbelow with reference to the sequence listing part.

[19028] VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19029] VGAM1362 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1362 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1362 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19030] The complementary binding of VGAM1362 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1362 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19031] It is appreciated that VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1362 host target genes. The mRNA of each one of this plurality of VGAM1362 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM1362 RNA, herein designated VGAM RNA, and which when bound by VGAM1362 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1362 host target proteins.

[19032] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1362 gene, herein designated VGAM GENE, on one or more VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19033] It is yet further appreciated that a function of VGAM1362 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1362 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM1362 correlate with, and may be deduced from, the identity of the host target genes which VGAM1362 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19034] Nucleotide sequences of the VGAM1362 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1362 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1362 are further described hereinbelow with reference to Table 1.

[19035] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1362 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19036] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1363 (VGAM1363) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19037] VGAM1363 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1363 was detected is described hereinabove with reference to Figs. 2–8.

[19038] VGAM1363 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM1363 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19039] VGAM1363 gene, herein designated VGAM GENE, encodes a VGAM1363 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1363 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1363 precursor RNA is designated SEQ ID:34784, and is provided hereinbelow with reference to the sequence listing part.

[19040] VGAM1363 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19041] An enzyme complex designated DICER COMPLEX, dices the VGAM1363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1363 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1363 RNA is designated SEQ ID:34785, and is provided hereinbelow with reference to the sequence listing part.

[19042] VGAM1363 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19043] VGAM1363 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1363 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19044] The complementary binding of VGAM1363 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1363 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19045] It is appreciated that VGAM1363 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1363 host target genes. The mRNA of each one of this plurality of VGAM1363 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1363 RNA, herein designated VGAM

RNA, and which when bound by VGAM1363 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1363 host target proteins.

[19046] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1363 gene, herein designated VGAM GENE, on one or more VGAM1363 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19047] It is yet further appreciated that a function of VGAM1363 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1363 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM1363 correlate with, and may be deduced from, the identity of the host target genes which VGAM1363 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19048] Nucleotide sequences of the VGAM1363 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1363 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1363 are further described hereinbelow with reference to Table 1.

[19049] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1363 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19050] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 1364 (VGAM1364) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19051] VGAM1364 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1364 was detected is described hereinabove with reference to Figs. 2-8.

[19052] VGAM1364 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19053] VGAM1364 gene, herein designated VGAM GENE, encodes a VGAM1364 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1364 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1364 precursor RNA is designated SEQ ID:34792, and is provided hereinbelow with reference to the sequence listing part.

[19054] VGAM1364 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19055] An enzyme complex designated DICER COMPLEX, dices the VGAM1364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1364 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1364 RNA is designated SEQ ID:34793, and is provided hereinbelow with reference to the sequence listing part.

[19056] VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19057] VGAM1364 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1364 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1364 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19058] The complementary binding of VGAM1364 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1364 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19059] It is appreciated that VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1364 host target genes. The mRNA of each one of this plurality of VGAM1364 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1364 RNA, herein designated VGAM RNA, and which when bound by VGAM1364 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1364 host target proteins.

[19060] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1364 gene, herein designated VGAM GENE, on one or more VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19061] It is yet further appreciated that a function of VGAM1364 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1364 include diagnosis, prevention and

treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM1364 correlate with, and may be deduced from, the identity of the host target genes which VGAM1364 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19062] Nucleotide sequences of the VGAM1364 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1364 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1364 are further described hereinbelow with reference to Table 1.

[19063] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1364 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19064] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1365 (VGAM1365) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19065] VGAM1365 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1365 was detected is described hereinabove with reference to Figs. 2–8.

[19066] VGAM1365 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 2. VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19067] VGAM1365 gene, herein designated VGAM GENE, encodes a VGAM1365 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1365 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1365 precursor RNA is designated SEQ ID:34799, and is provided hereinbelow with reference to the sequence listing part.

[19068] VGAM1365 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1365 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19069] An enzyme complex designated DICER COMPLEX, dices the VGAM1365 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1365 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1365 RNA is designated SEQ ID:34800, and is provided hereinbelow with reference to the sequence listing part.

[19070] VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1365 host target RNA, herein designated



VGAM HOST TARGET RNA. VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19071] VGAM1365 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1365 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19072] The complementary binding of VGAM1365 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1365 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19073] It is appreciated that VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1365 host target genes. The mRNA of each one of this plurality of VGAM1365 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1365 RNA, herein designated VGAM RNA, and which when bound by VGAM1365 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1365 host target proteins.

[19074] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1365 gene, herein designated VGAM GENE, on one or more VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19075] It is yet further appreciated that a function of VGAM1365 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 2. Spe-

cific functions, and accordingly utilities, of VGAM1365 correlate with, and may be deduced from, the identity of the host target genes which VGAM1365 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19076] Nucleotide sequences of the VGAM1365 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1365 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1365 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1365 are further described hereinbelow with reference to Table 1.

[19077] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1365 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19078] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1366 (VGAM1366) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[19079] VGAM1366 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1366 was detected is described hereinabove with reference to Figs. 2–8.

[19080] VGAM1366 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus. VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19081] VGAM1366 gene, herein designated VGAM GENE, encodes a VGAM1366 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1366 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1366 precursor RNA is designated SEQ ID:34989, and is provided hereinbelow with reference to the sequence listing part.

[19082] VGAM1366 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1366 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19083] An enzyme complex designated DICER COMPLEX, dices the VGAM1366 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1366 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1366 RNA is designated SEQ ID:34990, and is provided hereinbelow with reference to the sequence listing part.

[19084] VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1366 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19085] VGAM1366 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1366 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19086] The complementary binding of VGAM1366 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1366 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19087] It is appreciated that VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1366 host target genes. The mRNA of each one of this plurality of VGAM1366 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1366 RNA, herein designated VGAM RNA, and which when bound by VGAM1366 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1366 host target proteins.



[19088] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1366 gene, herein designated VGAM GENE, on one or more VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19089] It is yet further appreciated that a function of VGAM1366 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1366 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1366 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19090] Nucleotide sequences of the VGAM1366 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1366 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1366 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1366 are further described hereinbelow with reference to Table 1.

[19091] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1366 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19092] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1367 (VGAM1367) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[19093] VGAM1367 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1367 was detected is described hereinabove with reference to Figs. 2–8.

[19094] VGAM1367 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19095] VGAM1367 gene, herein designated VGAM GENE, encodes a VGAM1367 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1367 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1367 precursor RNA is designated SEQ ID:35098, and is provided hereinbelow with reference to the sequence listing part.

[19096] VGAM1367 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19097] An enzyme complex designated DICER COMPLEX, dices the VGAM1367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1367 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1367 RNA is designated SEQ ID:35099, and is provided hereinbelow with reference to the sequence listing part.

[19098] VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19099] VGAM1367 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1367 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1367 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19100] The complementary binding of VGAM1367 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1367 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19101] It is appreciated that VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1367 host target genes. The mRNA of each one of this plurality of VGAM1367 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1367 RNA, herein designated VGAM RNA, and which when bound by VGAM1367 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1367 host target proteins.

[19102] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1367 gene, herein designated VGAM GENE, on one or more VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19103] It is yet further appreciated that a function of VGAM1367 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1367 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM1367 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1367 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19104] Nucleotide sequences of the VGAM1367 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1367 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1367 are further described hereinbelow with reference to Table 1.

[19105] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1367 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19106] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1368 (VGAM1368) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[19107] VGAM1368 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1368 was detected is described hereinabove with reference to Figs. 2–8.

[19108] VGAM1368 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19109] VGAM1368 gene, herein designated VGAM GENE, encodes a VGAM1368 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1368 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1368 precursor RNA is designated SEQ ID:35117, and is provided hereinbelow with reference to the sequence listing part.

[19110] VGAM1368 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1368 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19111] An enzyme complex designated DICER COMPLEX, dices the VGAM1368 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1368 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1368 RNA is designated SEQ ID:35118, and is provided hereinbelow with reference to the sequence listing part.

[19112] VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19113] VGAM1368 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1368 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1368 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19114] The complementary binding of VGAM1368 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1368 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19115] It is appreciated that VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1368 host target genes. The mRNA of each one of this plurality of VGAM1368 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1368 RNA, herein designated VGAM RNA, and which when bound by VGAM1368 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1368 host target proteins.

[19116] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1368 gene, herein designated VGAM GENE, on one or more VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19117] It is yet further appreciated that a function of VGAM1368 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1368 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1368 correlate with, and may be deduced from, the identity of the host target genes which VGAM1368 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[19118] Nucleotide sequences of the VGAM1368 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1368 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1368 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1368 are further described hereinbelow with reference to Table 1.

[19119] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1368 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19120] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1369 (VGAM1369) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19121] VGAM1369 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1369 was detected is described hereinabove with reference to Figs. 2–8.

[19122] VGAM1369 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1369 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19123] VGAM1369 gene, herein designated VGAM GENE, encodes a VGAM1369 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1369 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1369 precursor RNA is designated SEQ ID:35174, and is provided hereinbelow with reference to the sequence listing part.

[19124] VGAM1369 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1369 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19125] An enzyme complex designated DICER COMPLEX, dices the VGAM1369 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1369 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1369 RNA is designated SEQ ID:7334, and is provided hereinbelow with reference to the sequence listing part.

[19126] VGAM1369 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and



a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19127] VGAM1369 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1369 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3'UTR and 5'UTR regions.

[19128] The complementary binding of VGAM1369 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1369 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19129] It is appreciated that VGAM1369 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1369 host target genes. The mRNA of each one of this plurality of VGAM1369 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1369 RNA, herein designated VGAM RNA, and which when bound by VGAM1369 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1369 host target proteins.

[19130] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1369 gene, herein designated VGAM GENE, on one or more VGAM1369 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19131] It is yet further appreciated that a function of VGAM1369 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1369 correlate with, and may be deduced from, the identity of the host target genes which VGAM1369 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[19132] Nucleotide sequences of the VGAM1369 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1369 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1369 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1369 are further described hereinbelow with reference to Table 1.

[19133] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1369 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19134] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1370 (VGAM1370) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19135] VGAM1370 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1370 was detected is described hereinabove with reference to Figs. 2–8.

[19136] VGAM1370 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19137] VGAM1370 gene, herein designated VGAM GENE, encodes a VGAM1370 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1370 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1370 precursor RNA is designated SEQ ID:35175, and is provided hereinbelow with reference to the sequence listing part.

[19138] VGAM1370 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19139] An enzyme complex designated DICER COMPLEX, dices the VGAM1370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1370 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1370 RNA is designated SEQ ID:7334, and is provided hereinbelow with reference to the sequence listing part.

[19140] VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[19141] VGAM1370 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1370 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19142] The complementary binding of VGAM1370 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1370 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19143] It is appreciated that VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1370 host target genes. The mRNA of each one of this plurality of VGAM1370 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1370 RNA, herein designated VGAM RNA, and which when bound by VGAM1370 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1370 host target proteins.

[19144] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1370 gene, herein designated VGAM GENE, on one



or more VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19145] It is yet further appreciated that a function of VGAM1370 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1370 correlate with, and may be deduced from, the identity of the host target genes which VGAM1370 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19146] Nucleotide sequences of the VGAM1370 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1370 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1370 are further described hereinbelow with reference to Table 1.

[19147] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1370 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19148] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1371 (VGAM1371) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19149] VGAM1371 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1371 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[19150] VGAM1371 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1371 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19151] VGAM1371 gene, herein designated VGAM GENE, encodes a VGAM1371 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1371 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1371 precursor RNA is designated SEQ ID:35176, and is provided hereinbelow with reference to the sequence listing part.

[19152] VGAM1371 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19153] An enzyme complex designated DICER COMPLEX, dices the VGAM1371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1371 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1371 RNA is designated SEQ ID:35177, and is provided hereinbelow with reference to the sequence listing part.

[19154] VGAM1371 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19155] VGAM1371 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1371 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1371 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19156] The complementary binding of VGAM1371 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1371 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19157] It is appreciated that VGAM1371 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1371 host target genes. The mRNA of each one of this plurality of VGAM1371 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1371 RNA, herein designated VGAM RNA, and which when bound by VGAM1371 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1371 host target proteins.

[19158] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1371 gene, herein designated VGAM GENE, on one or more VGAM1371 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19159] It is yet further appreciated that a function of VGAM1371 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1371 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1371 correlate with, and may be deduced from, the identity of the host target genes which VGAM1371 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19160] Nucleotide sequences of the VGAM1371 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1371 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1371 are further described hereinbelow with reference to Table 1.

[19161] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1371 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19162] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1372 (VGAM1372) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19163] VGAM1372 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1372 was detected is described hereinabove with reference to Figs. 2-8.



[19164] VGAM1372 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19165] VGAM1372 gene, herein designated VGAM GENE, encodes a VGAM1372 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1372 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1372 precursor RNA is designated SEQ ID:35304, and is provided hereinbelow with reference to the sequence listing part.

[19166] VGAM1372 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[19167] An enzyme complex designated DICER COMPLEX, dices the VGAM1372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1372 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1372 RNA is designated SEQ ID:35305, and is provided hereinbelow with reference to the sequence listing part.

[19168] VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19169] VGAM1372 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1372 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19170] The complementary binding of VGAM1372 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1372 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19171] It is appreciated that VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1372 host target genes. The mRNA of each one of this plurality of VGAM1372 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1372 RNA, herein designated VGAM RNA, and which when bound by VGAM1372 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1372 host target proteins.

[19172] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1372 gene, herein designated VGAM GENE, on one or more VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19173] It is yet further appreciated that a function of VGAM1372 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1372 correlate with, and may be deduced from, the identity of the host target genes which VGAM1372 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19174] Nucleotide sequences of the VGAM1372 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1372 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1372 are further described hereinbelow with reference to Table 1.

[19175] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1372 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19176] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1373 (VGAM1373) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19177] VGAM1373 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1373 was detected is described hereinabove with reference to Figs. 2-8.

[19178] VGAM1373 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Tupaia herpesvirus. VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19179] VGAM1373 gene, herein designated VGAM GENE, encodes a VGAM1373 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1373 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1373 precursor RNA is designated SEQ ID:35335, and is provided hereinbelow with reference to the sequence listing part.

[19180] VGAM1373 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19181] An enzyme complex designated DICER COMPLEX, dices the VGAM1373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1373 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1373 RNA is designated SEQ ID:35336, and is provided hereinbelow with reference to the sequence listing part.

[19182] VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19183] VGAM1373 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites



located in untranslated regions of VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1373 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19184] The complementary binding of VGAM1373 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1373 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1373 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19185] It is appreciated that VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1373 host target genes. The mRNA of each one of this plurality of VGAM1373 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1373 RNA, herein designated VGAM RNA, and which when bound by VGAM1373 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1373 host target proteins.

[19186] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1373 gene, herein designated VGAM GENE, on one or more VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19187] It is yet further appreciated that a function of VGAM1373 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1373 correlate with, and may be deduced from, the identity of the host target genes which VGAM1373 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19188] Nucleotide sequences of the VGAM1373 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1373 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1373 are further described hereinbelow with reference to Table 1.

[19189] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1373 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19190] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1374 (VGAM1374) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19191] VGAM1374 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1374 was detected is described hereinabove with reference to Figs. 2-8.

[19192] VGAM1374 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19193] VGAM1374 gene, herein designated VGAM GENE, encodes a VGAM1374 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1374 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1374 precursor RNA is designated SEQ ID:35405, and is provided hereinbelow with reference to the sequence listing part.

[19194] VGAM1374 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19195] An enzyme complex designated DICER COMPLEX, dices

the VGAM1374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1374 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1374 RNA is designated SEQ ID:35406, and is provided hereinbelow with reference to the sequence listing part.

[19196] VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19197] VGAM1374 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1374 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1374 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1374 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19198] The complementary binding of VGAM1374 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1374 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19199] It is appreciated that VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1374 host target genes. The mRNA of each one of this plurality of VGAM1374 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1374 RNA, herein designated VGAM RNA, and which when bound by VGAM1374 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1374 host target proteins.

[19200] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1374 gene, herein designated VGAM GENE, on one or more VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19201] It is yet further appreciated that a function of VGAM1374 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1374 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1374 correlate with, and may be deduced from, the identity of the host target genes which VGAM1374 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19202] Nucleotide sequences of the VGAM1374 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1374 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1374 are further described hereinbelow with reference to Table 1.

[19203] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1374 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19204] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1375 (VGAM1375) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19205] VGAM1375 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1375 was detected is described hereinabove with reference to Figs. 2-8.

[19206] VGAM1375 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1375 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[19207] VGAM1375 gene, herein designated VGAM GENE, encodes a VGAM1375 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1375 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1375 precursor RNA is designated SEQ ID:35410, and is provided hereinbelow with reference to the sequence listing part.

[19208] VGAM1375 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1375 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19209] An enzyme complex designated DICER COMPLEX, dices the VGAM1375 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1375 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1375 RNA is designated SEQ ID:35411, and is provided hereinbelow with reference to the sequence listing part.

[19210] VGAM1375 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19211] VGAM1375 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1375 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19212] The complementary binding of VGAM1375 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1375

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1375 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19213] It is appreciated that VGAM1375 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1375 host target genes. The mRNA of each one of this plurality of VGAM1375 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1375 RNA, herein designated VGAM RNA, and which when bound by VGAM1375 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1375 host target proteins.

[19214] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1375 gene, herein designated VGAM GENE, on one or more VGAM1375 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19215] It is yet further appreciated that a function of VGAM1375 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1375 correlate with, and may be deduced from, the identity of the host target genes which VGAM1375 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19216] Nucleotide sequences of the VGAM1375 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1375 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1375 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1375 are further described hereinbelow with reference to Table 1.

[19217] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1375 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19218] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1376 (VGAM1376) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19219] VGAM1376 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1376 was detected is described hereinabove with reference to Figs. 2-8.

[19220] VGAM1376 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[19221] VGAM1376 gene, herein designated VGAM GENE, encodes a VGAM1376 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1376 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1376 precursor RNA is designated SEQ ID:35452, and is provided hereinbelow with reference to the sequence listing part.

[19222] VGAM1376 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19223] An enzyme complex designated DICER COMPLEX, dices the VGAM1376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1376 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1376 RNA is designated SEQ ID:35453, and is provided hereinbelow with reference to the sequence listing part.

[19224] VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19225] VGAM1376 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1376 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19226] The complementary binding of VGAM1376 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1376 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1376 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19227] It is appreciated that VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1376 host target genes. The mRNA of each one of this plurality of VGAM1376 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1376 RNA, herein designated VGAM RNA, and which when bound by VGAM1376 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1376 host target proteins.

[19228] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1376 gene, herein designated VGAM GENE, on one or more VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19229] It is yet further appreciated that a function of VGAM1376 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1376 correlate with, and may be deduced from, the identity of the host target genes which VGAM1376 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19230] Nucleotide sequences of the VGAM1376 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1376 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1376 are further

described hereinbelow with reference to Table 1.

[19231] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1376 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19232] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1377 (VGAM1377) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19233] VGAM1377 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1377 was detected is described hereinabove with reference to Figs. 2-8.

[19234] VGAM1377 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus. VGAM1377 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19235] VGAM1377 gene, herein designated VGAM GENE, encodes a VGAM1377 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1377 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1377 precursor RNA is designated SEQ ID:35486, and is provided hereinbelow with reference to the sequence listing part.

[19236] VGAM1377 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1377 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19237] An enzyme complex designated DICER COMPLEX, dices the VGAM1377 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1377 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1377 RNA is designated SEQ ID:35487, and is provided hereinbelow with reference to the sequence listing part.

[19238] VGAM1377 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19239] VGAM1377 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1377 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1377 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19240] The complementary binding of VGAM1377 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1377 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19241] It is appreciated that VGAM1377 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1377 host target genes. The mRNA of each one of this plurality of VGAM1377 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1377 RNA, herein designated VGAM RNA, and which when bound by VGAM1377 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1377 host target proteins.

[19242] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1377 gene, herein designated VGAM GENE, on one or more VGAM1377 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19243] It is yet further appreciated that a function of VGAM1377 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1377 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM1377 correlate with, and may be deduced from, the identity of the host target genes which VGAM1377 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19244] Nucleotide sequences of the VGAM1377 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1377 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1377 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1377 are further described hereinbelow with reference to Table 1.

[19245] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1377 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19246] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1378 (VGAM1378) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19247] VGAM1378 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1378 was detected is described hereinabove with reference to Figs. 2-8.

[19248] VGAM1378 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma virus. VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19249] VGAM1378 gene, herein designated VGAM GENE, encodes

a VGAM1378 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1378 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1378 precursor RNA is designated SEQ ID:35491, and is provided hereinbelow with reference to the sequence listing part.

[19250] VGAM1378 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19251] An enzyme complex designated DICER COMPLEX, dices the VGAM1378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1378 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1378 RNA is designated SEQ ID:35492, and is provided hereinbelow with reference to the sequence listing part.

[19252] VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19253] VGAM1378 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1378 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19254] The complementary binding of VGAM1378 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1378 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[19255] It is appreciated that VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1378 host target genes. The mRNA of each one of this plurality of VGAM1378 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1378 RNA, herein designated VGAM RNA, and which when bound by VGAM1378 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1378 host target proteins.

[19256] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1378 gene, herein designated VGAM GENE, on one or more VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19257] It is yet further appreciated that a function of VGAM1378 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of viral infection by Myxoma virus. Specific functions, and accordingly utilities, of VGAM1378 correlate with, and may be deduced from, the identity of the host target genes which VGAM1378 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19258] Nucleotide sequences of the VGAM1378 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1378 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1378 are further described hereinbelow with reference to Table 1.

[19259] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1378 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19260] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1379 (VGAM1379) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19261] VGAM1379 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1379 was detected is described hereinabove with reference to Figs. 2-8.

[19262] VGAM1379 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1379 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19263] VGAM1379 gene, herein designated VGAM GENE, encodes a VGAM1379 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1379 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1379 precursor RNA is designated SEQ ID:35498, and is provided hereinbelow with reference to the sequence listing part.

[19264] VGAM1379 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19265] An enzyme complex designated DICER COMPLEX, dices the VGAM1379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1379 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1379 RNA is designated SEQ ID:35499, and is provided hereinbelow with reference to the sequence listing part.

[19266] VGAM1379 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19267] VGAM1379 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1379 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1379 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19268] The complementary binding of VGAM1379 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1379 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19269] It is appreciated that VGAM1379 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1379 host target genes. The mRNA of each one of this plurality of VGAM1379 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1379 RNA, herein designated VGAM RNA, and which when bound by VGAM1379 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1379 host target proteins.

[19270] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1379 gene, herein designated VGAM GENE, on one or more VGAM1379 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19271] It is yet further appreciated that a function of VGAM1379 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1379 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1379 correlate with, and may be deduced from, the identity of the host target genes which VGAM1379 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19272] Nucleotide sequences of the VGAM1379 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1379 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1379 are further described hereinbelow with reference to Table 1.

[19273] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1379 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19274] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1380 (VGAM1380) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19275] VGAM1380 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1380 was detected is described hereinabove with reference to Figs. 2-8.

[19276] VGAM1380 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Visna virus. VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19277] VGAM1380 gene, herein designated VGAM GENE, encodes a VGAM1380 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1380 precursor RNA,



herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1380 precursor RNA is designated SEQ ID:35517, and is provided hereinbelow with reference to the sequence listing part.

[19278] VGAM1380 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19279] An enzyme complex designated DICER COMPLEX, dices the VGAM1380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1380 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1380 RNA is designated SEQ ID:35518, and is provided hereinbelow with reference to the sequence listing part.

[19280] VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19281] VGAM1380 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1380 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1380 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19282] The complementary binding of VGAM1380 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1380 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19283] It is appreciated that VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1380 host target genes. The mRNA of each one of this plurality of VGAM1380 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1380 RNA, herein designated VGAM RNA, and which when bound by VGAM1380 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1380 host target proteins.

[19284] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1380 gene, herein designated VGAM GENE, on one or more VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[19285] It is yet further appreciated that a function of VGAM1380 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1380 include diagnosis, prevention and treatment of viral infection by Visna virus. Specific functions, and accordingly utilities, of VGAM1380 correlate with, and may be deduced from, the identity of the host target genes which VGAM1380 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19286] Nucleotide sequences of the VGAM1380 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1380 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1380 are further described hereinbelow with reference to Table 1.

[19287] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1380 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19288] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1381 (VGAM1381) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19289] VGAM1381 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1381 was detected is described hereinabove with reference to Figs. 2-8.

[19290] VGAM1381 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19291] VGAM1381 gene, herein designated VGAM GENE, encodes a VGAM1381 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1381 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1381 precursor RNA is designated SEQ ID:35607, and is provided hereinbelow with reference to the sequence listing part.

[19292] VGAM1381 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19293] An enzyme complex designated DICER COMPLEX, dices the VGAM1381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1381 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1381 RNA is designated SEQ ID:35608, and is provided hereinbelow with reference to the sequence listing part.

[19294] VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19295] VGAM1381 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1381 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-



preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1381 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19296] The complementary binding of VGAM1381 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1381 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19297] It is appreciated that VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1381 host target genes. The mRNA of

each one of this plurality of VGAM1381 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1381 RNA, herein designated VGAM RNA, and which when bound by VGAM1381 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1381 host target proteins.

[19298] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1381 gene, herein designated VGAM GENE, on one or more VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[19299] It is yet further appreciated that a function of VGAM1381 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1381 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1381 correlate with, and may be deduced from, the identity of the host target genes which VGAM1381 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19300] Nucleotide sequences of the VGAM1381 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1381 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1381 are further described hereinbelow with reference to Table 1.

[19301] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1381 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[19302] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1382 (VGAM1382) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19303] VGAM1382 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1382 was detected is described hereinabove with reference to Figs. 2–8.

[19304] VGAM1382 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19305] VGAM1382 gene, herein designated VGAM GENE, encodes a VGAM1382 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1382 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1382 precursor RNA is designated SEQ ID:35616, and is provided hereinbelow with reference to the sequence listing part.

[19306] VGAM1382 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19307] An enzyme complex designated DICER COMPLEX, dices the VGAM1382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1382 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1382 RNA is designated SEQ ID:35617,

and is provided hereinbelow with reference to the sequence listing part.

[19308] VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19309] VGAM1382 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1382 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19310] The complementary binding of VGAM1382 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1382 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19311] It is appreciated that VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1382 host target genes. The mRNA of each one of this plurality of VGAM1382 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1382 RNA, herein designated VGAM RNA, and which when bound by VGAM1382 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1382 host target proteins.

[19312] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1382 gene, herein designated VGAM GENE, on one or more VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).



[19313] It is yet further appreciated that a function of VGAM1382 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1382 correlate with, and may be deduced from, the identity of the host target genes which VGAM1382 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19314] Nucleotide sequences of the VGAM1382 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1382 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1382 are further described hereinbelow with reference to Table 1.

[19315] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1382 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19316] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1383 (VGAM1383) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19317] VGAM1383 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1383 was detected is described hereinabove with reference to Figs. 2–8.

[19318] VGAM1383 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Visna virus. VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19319] VGAM1383 gene, herein designated VGAM GENE, encodes a VGAM1383 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1383 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1383 precursor RNA is designated SEQ ID:35624, and is provided

hereinbelow with reference to the sequence listing part.

[19320] VGAM1383 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19321] An enzyme complex designated DICER COMPLEX, dices the VGAM1383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1383 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1383 RNA is designated SEQ ID:35625, and is provided hereinbelow with reference to the sequence listing part.

[19322] VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19323] VGAM1383 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1383 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19324] The complementary binding of VGAM1383 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1383 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19325] It is appreciated that VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1383 host target genes. The mRNA of each one of this plurality of VGAM1383 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1383 RNA, herein designated VGAM RNA, and which when bound by VGAM1383 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1383 host target proteins.

[19326] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1383 gene, herein designated VGAM GENE, on one or more VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19327] It is yet further appreciated that a function of VGAM1383 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of viral infection by Visna virus. Specific functions, and accordingly utilities, of VGAM1383 correlate with, and may be deduced from, the identity of the host target genes which VGAM1383 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19328] Nucleotide sequences of the VGAM1383 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1383 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1383 are further described hereinbelow with reference to Table 1.

[19329] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1383 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19330] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1384 (VGAM1384) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19331] VGAM1384 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1384 was detected is described hereinabove with reference to Figs. 2–8.

[19332] VGAM1384 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Visna virus. VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19333] VGAM1384 gene, herein designated VGAM GENE, encodes a VGAM1384 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1384 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1384 precursor RNA is designated SEQ ID:35672, and is provided hereinbelow with reference to the sequence listing part.

[19334] VGAM1384 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM1384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19335] An enzyme complex designated DICER COMPLEX, dices the VGAM1384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1384 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1384 RNA is designated SEQ ID:35673, and is provided hereinbelow with reference to the sequence listing part.

[19336] VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19337] VGAM1384 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1384 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1384 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19338] The complementary binding of VGAM1384 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1384 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19339] It is appreciated that VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1384 host target genes. The mRNA of each one of this plurality of VGAM1384 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1384 RNA, herein designated VGAM RNA, and which when bound by VGAM1384 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1384 host target proteins.

[19340] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1384 gene, herein designated VGAM GENE, on one or more VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19341] It is yet further appreciated that a function of VGAM1384 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1384 include diagnosis, prevention and

treatment of viral infection by Visna virus. Specific functions, and accordingly utilities, of VGAM1384 correlate with, and may be deduced from, the identity of the host target genes which VGAM1384 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19342] Nucleotide sequences of the VGAM1384 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1384 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1384 are further described hereinbelow with reference to Table 1.

[19343] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1384 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19344] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1385 (VGAM1385) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19345] VGAM1385 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1385 was detected is described hereinabove with reference to Figs. 2–8.

[19346] VGAM1385 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19347] VGAM1385 gene, herein designated VGAM GENE, encodes a VGAM1385 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1385 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1385 precursor RNA is designated SEQ ID:35679, and is provided hereinbelow with reference to the sequence listing part.

[19348] VGAM1385 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1385 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19349] An enzyme complex designated DICER COMPLEX, dices the VGAM1385 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1385 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1385 RNA is designated SEQ ID:35680, and is provided hereinbelow with reference to the sequence listing part.

[19350] VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1385 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19351] VGAM1385 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1385 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1385 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19352] The complementary binding of VGAM1385 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1385 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19353] It is appreciated that VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1385 host target genes. The mRNA of each one of this plurality of VGAM1385 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1385 RNA, herein designated VGAM RNA, and which when bound by VGAM1385 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1385 host target proteins.

[19354] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1385 gene, herein designated VGAM GENE, on one or more VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19355] It is yet further appreciated that a function of VGAM1385 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1385 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific

functions, and accordingly utilities, of VGAM1385 correlate with, and may be deduced from, the identity of the host target genes which VGAM1385 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19356] Nucleotide sequences of the VGAM1385 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1385 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1385 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1385 are further described hereinbelow with reference to Table 1.

[19357] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1385 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19358] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1386 (VGAM1386) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[19359] VGAM1386 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1386 was detected is described hereinabove with reference to Figs. 2–8.

[19360] VGAM1386 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19361] VGAM1386 gene, herein designated VGAM GENE, encodes a VGAM1386 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1386 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1386 precursor RNA is designated SEQ ID:35693, and is provided hereinbelow with reference to the sequence listing part.

[19362] VGAM1386 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1386 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19363] An enzyme complex designated DICER COMPLEX, dices the VGAM1386 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1386 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1386 RNA is designated SEQ ID:35694, and is provided hereinbelow with reference to the sequence listing part.

[19364] VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1386 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19365] VGAM1386 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1386 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19366] The complementary binding of VGAM1386 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1386 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19367] It is appreciated that VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1386 host target genes. The mRNA of each one of this plurality of VGAM1386 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1386 RNA, herein designated VGAM RNA, and which when bound by VGAM1386 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1386 host target proteins.

[19368] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1386 gene, herein designated VGAM GENE, on one or more VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19369] It is yet further appreciated that a function of VGAM1386 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities,



of VGAM1386 correlate with, and may be deduced from, the identity of the host target genes which VGAM1386 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19370] Nucleotide sequences of the VGAM1386 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1386 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1386 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1386 are further described hereinbelow with reference to Table 1.

[19371] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1386 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19372] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1387 (VGAM1387) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[19373] VGAM1387 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1387 was detected is described hereinabove with reference to Figs. 2–8.

[19374] VGAM1387 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox virus. VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19375] VGAM1387 gene, herein designated VGAM GENE, encodes a VGAM1387 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1387 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1387 precursor RNA is designated SEQ ID:35706, and is provided hereinbelow with reference to the sequence listing part.

[19376] VGAM1387 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19377] An enzyme complex designated DICER COMPLEX, dices the VGAM1387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1387 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1387 RNA is designated SEQ ID:35707, and is provided hereinbelow with reference to the sequence listing part.

[19378] VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19379] VGAM1387 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1387 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[19380] The complementary binding of VGAM1387 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1387 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19381] It is appreciated that VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1387 host target genes. The mRNA of each one of this plurality of VGAM1387 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1387 RNA, herein designated VGAM RNA, and which when bound by VGAM1387 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1387 host target proteins.

[19382] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1387 gene, herein designated VGAM GENE, on one

or more VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19383] It is yet further appreciated that a function of VGAM1387 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific functions, and accordingly utilities, of VGAM1387 correlate with, and may be deduced from, the identity of the host target genes which VGAM1387 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19384] Nucleotide sequences of the VGAM1387 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1387 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1387 are further described hereinbelow with reference to Table 1.

[19385] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1387 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19386] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1388 (VGAM1388) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19387] VGAM1388 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1388 was detected is de-



scribed hereinabove with reference to Figs. 2–8.

[19388] VGAM1388 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ovine lentivirus.

VGAM1388 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19389] VGAM1388 gene, herein designated VGAM GENE, encodes a VGAM1388 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1388 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1388 precursor RNA is designated SEQ ID:35712, and is provided hereinbelow with reference to the sequence listing part.

[19390] VGAM1388 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1388 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19391] An enzyme complex designated DICER COMPLEX, dices the VGAM1388 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1388 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1388 RNA is designated SEQ ID:35713, and is provided hereinbelow with reference to the sequence listing part.

[19392] VGAM1388 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19393] VGAM1388 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1388 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1388 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19394] The complementary binding of VGAM1388 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1388 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19395] It is appreciated that VGAM1388 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1388 host target genes. The mRNA of each one of this plurality of VGAM1388 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1388 RNA, herein designated VGAM RNA, and which when bound by VGAM1388 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1388 host target proteins.

[19396] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1388 gene, herein designated VGAM GENE, on one or more VGAM1388 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19397] It is yet further appreciated that a function of VGAM1388 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1388 include diagnosis, prevention and treatment of viral infection by Ovine lentivirus. Specific functions, and accordingly utilities, of VGAM1388 correlate with, and may be deduced from, the identity of the host target genes which VGAM1388 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19398] Nucleotide sequences of the VGAM1388 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1388 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1388 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1388 are further described hereinbelow with reference to Table 1.

[19399] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1388 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19400] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1389 (VGAM1389) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19401] VGAM1389 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1389 was detected is described hereinabove with reference to Figs. 2-8.

[19402] VGAM1389 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19403] VGAM1389 gene, herein designated VGAM GENE, encodes a VGAM1389 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1389 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1389 precursor RNA is designated SEQ ID:35721, and is provided hereinbelow with reference to the sequence listing part.

[19404] VGAM1389 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[19405] An enzyme complex designated DICER COMPLEX, dices the VGAM1389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1389 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1389 RNA is designated SEQ ID:35722, and is provided hereinbelow with reference to the sequence listing part.

[19406] VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19407] VGAM1389 RNA, herein designated VGAM RNA, binds



complementarily to one or more host target binding sites located in untranslated regions of VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1389 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19408] The complementary binding of VGAM1389 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1389 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19409] It is appreciated that VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1389 host target genes. The mRNA of each one of this plurality of VGAM1389 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1389 RNA, herein designated VGAM RNA, and which when bound by VGAM1389 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1389 host target proteins.

[19410] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1389 gene, herein designated VGAM GENE, on one or more VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19411] It is yet further appreciated that a function of VGAM1389 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1389 correlate with, and may be deduced from, the identity of the host target genes which VGAM1389 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19412] Nucleotide sequences of the VGAM1389 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1389 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1389 are further described hereinbelow with reference to Table 1.

[19413] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1389 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19414] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1390 (VGAM1390) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19415] VGAM1390 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1390 was detected is described hereinabove with reference to Figs. 2-8.

[19416] VGAM1390 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Sheeppox virus.

VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19417] VGAM1390 gene, herein designated VGAM GENE, encodes a VGAM1390 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1390 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1390 precursor RNA is designated SEQ ID:35744, and is provided hereinbelow with reference to the sequence listing part.

[19418] VGAM1390 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1390 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19419] An enzyme complex designated DICER COMPLEX, dices the VGAM1390 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1390 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1390 RNA is designated SEQ ID:35745, and is provided hereinbelow with reference to the sequence listing part.

[19420] VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19421] VGAM1390 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1390 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1390 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19422] The complementary binding of VGAM1390 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1390 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1390 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19423] It is appreciated that VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1390 host target genes. The mRNA of each one of this plurality of VGAM1390 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1390 RNA, herein designated VGAM RNA, and which when bound by VGAM1390 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1390 host target proteins.

[19424] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1390 gene, herein designated VGAM GENE, on one or more VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove



with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19425] It is yet further appreciated that a function of VGAM1390 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1390 include diagnosis, prevention and treatment of viral infection by Sheeppox virus. Specific functions, and accordingly utilities, of VGAM1390 correlate with, and may be deduced from, the identity of the host target genes which VGAM1390 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19426] Nucleotide sequences of the VGAM1390 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1390 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1390 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1390 are further described hereinbelow with reference to Table 1.

[19427] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1390 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19428] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1391 (VGAM1391) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19429] VGAM1391 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1391 was detected is described hereinabove with reference to Figs. 2-8.

[19430] VGAM1391 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Melanoplus sanguinipes*

entomopoxvirus. VGAM1391 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19431] VGAM1391 gene, herein designated VGAM GENE, encodes a VGAM1391 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1391 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1391 precursor RNA is designated SEQ ID:35753, and is provided hereinbelow with reference to the sequence listing part.

[19432] VGAM1391 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1391 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19433] An enzyme complex designated DICER COMPLEX, dices

the VGAM1391 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1391 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1391 RNA is designated SEQ ID:35754, and is provided hereinbelow with reference to the sequence listing part.

[19434] VGAM1391 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19435] VGAM1391 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1391 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1391 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19436] The complementary binding of VGAM1391 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1391 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19437] It is appreciated that VGAM1391 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1391 host target genes. The mRNA of each one of this plurality of VGAM1391 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1391 RNA, herein designated VGAM RNA, and which when bound by VGAM1391 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1391 host target proteins.

[19438] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1391 gene, herein designated VGAM GENE, on one or more VGAM1391 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19439] It is yet further appreciated that a function of VGAM1391 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1391 correlate with, and may be deduced from, the identity of the host target genes which VGAM1391 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19440] Nucleotide sequences of the VGAM1391 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1391 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1391 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1391 are further described hereinbelow with reference to Table 1.

[19441] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1391 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19442] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1392 (VGAM1392) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19443] VGAM1392 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1392 was detected is described hereinabove with reference to Figs. 2-8.

[19444] VGAM1392 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1392 host target gene, herein



designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19445] VGAM1392 gene, herein designated VGAM GENE, encodes a VGAM1392 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1392 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1392 precursor RNA is designated SEQ ID:35758, and is provided hereinbelow with reference to the sequence listing part.

[19446] VGAM1392 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1392 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19447] An enzyme complex designated DICER COMPLEX, dices the VGAM1392 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1392 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1392 RNA is designated SEQ ID:35759, and is provided hereinbelow with reference to the sequence listing part.

[19448] VGAM1392 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19449] VGAM1392 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1392 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19450] The complementary binding of VGAM1392 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1392

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1392 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19451] It is appreciated that VGAM1392 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1392 host target genes. The mRNA of each one of this plurality of VGAM1392 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1392 RNA, herein designated VGAM RNA, and which when bound by VGAM1392 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1392 host target proteins.

[19452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1392 gene, herein designated VGAM GENE, on one or more VGAM1392 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19453] It is yet further appreciated that a function of VGAM1392 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1392 correlate with, and may be deduced from, the identity of the host target genes which VGAM1392 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19454] Nucleotide sequences of the VGAM1392 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1392 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1392 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1392 are further described hereinbelow with reference to Table 1.

[19455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1392 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19456] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1393 (VGAM1393) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19457] VGAM1393 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1393 was detected is described hereinabove with reference to Figs. 2-8.

[19458] VGAM1393 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ovine lentivirus. VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[19459] VGAM1393 gene, herein designated VGAM GENE, encodes a VGAM1393 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1393 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1393 precursor RNA is designated SEQ ID:35763, and is provided hereinbelow with reference to the sequence listing part.

[19460] VGAM1393 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19461] An enzyme complex designated DICER COMPLEX, dices the VGAM1393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1393 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1393 RNA is designated SEQ ID:35764, and is provided hereinbelow with reference to the sequence listing part.

[19462] VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19463] VGAM1393 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-



cleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1393 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19464] The complementary binding of VGAM1393 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1393 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1393 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19465] It is appreciated that VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1393 host target genes. The mRNA of each one of this plurality of VGAM1393 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1393 RNA, herein designated VGAM RNA, and which when bound by VGAM1393 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1393 host target proteins.

[19466] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1393 gene, herein designated VGAM GENE, on one or more VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19467] It is yet further appreciated that a function of VGAM1393 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of viral infection by Ovine lentivirus. Specific functions, and accordingly utilities, of VGAM1393 correlate with, and may be deduced from, the identity of the host target genes which VGAM1393 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19468] Nucleotide sequences of the VGAM1393 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1393 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1393 are further

described hereinbelow with reference to Table 1.

[19469] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1393 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19470] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1394 (VGAM1394) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19471] VGAM1394 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1394 was detected is described hereinabove with reference to Figs. 2-8.

[19472] VGAM1394 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Carnation mottle virus. VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19473] VGAM1394 gene, herein designated VGAM GENE, encodes a VGAM1394 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1394 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1394 precursor RNA is designated SEQ ID:35778, and is provided hereinbelow with reference to the sequence listing part.

[19474] VGAM1394 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19475] An enzyme complex designated DICER COMPLEX, dices the VGAM1394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1394 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1394 RNA is designated SEQ ID:35779, and is provided hereinbelow with reference to the sequence listing part.

[19476] VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19477] VGAM1394 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1394 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1394 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19478] The complementary binding of VGAM1394 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1394 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19479] It is appreciated that VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1394 host target genes. The mRNA of each one of this plurality of VGAM1394 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1394 RNA, herein designated VGAM RNA, and which when bound by VGAM1394 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1394 host target proteins.

[19480] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1394 gene, herein designated VGAM GENE, on one or more VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are



also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19481] It is yet further appreciated that a function of VGAM1394 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of viral infection by Carnation mottle virus. Specific functions, and accordingly utilities, of VGAM1394 correlate with, and may be deduced from, the identity of the host target genes which VGAM1394 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19482] Nucleotide sequences of the VGAM1394 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1394 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1394 are further described hereinbelow with reference to Table 1.

[19483] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1394 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19484] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1395 (VGAM1395) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19485] VGAM1395 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1395 was detected is described hereinabove with reference to Figs. 2-8.

[19486] VGAM1395 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Carnation mottle virus. VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19487] VGAM1395 gene, herein designated VGAM GENE, encodes

a VGAM1395 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1395 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1395 precursor RNA is designated SEQ ID:35786, and is provided hereinbelow with reference to the sequence listing part.

[19488] VGAM1395 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19489] An enzyme complex designated DICER COMPLEX, dices the VGAM1395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1395 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1395 RNA is designated SEQ ID:35787, and is provided hereinbelow with reference to the sequence listing part.

[19490] VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19491] VGAM1395 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1395 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19492] The complementary binding of VGAM1395 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1395 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[19493] It is appreciated that VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1395 host target genes. The mRNA of each one of this plurality of VGAM1395 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1395 RNA, herein designated VGAM RNA, and which when bound by VGAM1395 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1395 host target proteins.

[19494] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1395 gene, herein designated VGAM GENE, on one or more VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19495] It is yet further appreciated that a function of VGAM1395 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of viral infection by Carnation mottle virus. Specific functions, and accordingly utilities, of VGAM1395 correlate with, and may be deduced from, the identity of the host target genes which VGAM1395 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19496] Nucleotide sequences of the VGAM1395 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1395 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1395 are further described hereinbelow with reference to Table 1.

[19497] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1395 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19498] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1396 (VGAM1396) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19499] VGAM1396 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1396 was detected is described hereinabove with reference to Figs. 2-8.

[19500] VGAM1396 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Carnation mottle virus. VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19501] VGAM1396 gene, herein designated VGAM GENE, encodes a VGAM1396 precursor RNA, herein designated VGAM



PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1396 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1396 precursor RNA is designated SEQ ID:35792, and is provided hereinbelow with reference to the sequence listing part.

[19502] VGAM1396 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19503] An enzyme complex designated DICER COMPLEX, dices the VGAM1396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1396 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1396 RNA is designated SEQ ID:35793, and is provided hereinbelow with reference to the sequence listing part.

[19504] VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19505] VGAM1396 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1396 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19506] The complementary binding of VGAM1396 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1396 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19507] It is appreciated that VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1396 host target genes. The mRNA of each one of this plurality of VGAM1396 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1396 RNA, herein designated VGAM RNA, and which when bound by VGAM1396 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1396 host target proteins.

[19508] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1396 gene, herein designated VGAM GENE, on one or more VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19509] It is yet further appreciated that a function of VGAM1396 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of viral infection by Carnation mottle virus. Specific functions, and accordingly utilities, of VGAM1396 correlate with, and may be deduced from, the identity of the host target genes which VGAM1396 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19510] Nucleotide sequences of the VGAM1396 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1396 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1396 are further described hereinbelow with reference to Table 1.

[19511] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1396 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19512] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1397 (VGAM1397) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19513] VGAM1397 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1397 was detected is described hereinabove with reference to Figs. 2-8.

[19514] VGAM1397 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Caprine arthritis-encephalitis virus. VGAM1397 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19515] VGAM1397 gene, herein designated VGAM GENE, encodes a VGAM1397 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1397 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1397 precursor RNA is designated SEQ ID:35802, and is provided hereinbelow with reference to the sequence listing part.

[19516] VGAM1397 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1397 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19517] An enzyme complex designated DICER COMPLEX, dices the VGAM1397 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1397 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1397 RNA is designated SEQ ID:35803, and is provided hereinbelow with reference to the sequence listing part.

[19518] VGAM1397 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19519] VGAM1397 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3



such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1397 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19520] The complementary binding of VGAM1397 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1397 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19521] It is appreciated that VGAM1397 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1397 host target genes. The mRNA of each one of this plurality of VGAM1397 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1397 RNA, herein designated VGAM RNA, and which when bound by VGAM1397 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1397 host target proteins.

[19522] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1397 gene, herein designated VGAM GENE, on one or more VGAM1397 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19523] It is yet further appreciated that a function of VGAM1397 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of viral infection by Caprine arthritis–encephalitis virus. Specific functions, and accordingly utilities, of VGAM1397 correlate with, and may be deduced from, the identity of the host target genes which VGAM1397 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19524] Nucleotide sequences of the VGAM1397 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1397 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1397 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1397 are further described hereinbelow with reference to Table 1.

[19525] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1397 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19526] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1398 (VGAM1398) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19527] VGAM1398 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1398 was detected is described hereinabove with reference to Figs. 2–8.

[19528] VGAM1398 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Caprine arthritis–encephalitis virus. VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19529] VGAM1398 gene, herein designated VGAM GENE, encodes a VGAM1398 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1398 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1398 precursor RNA is designated SEQ ID:35854, and is provided hereinbelow with reference to the sequence listing part.

[19530] VGAM1398 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19531] An enzyme complex designated DICER COMPLEX, dices the VGAM1398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1398 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1398 RNA is designated SEQ ID:35855, and is provided hereinbelow with reference to the sequence listing part.

[19532] VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19533] VGAM1398 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1398 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19534] The complementary binding of VGAM1398 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1398 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19535] It is appreciated that VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1398 host target genes. The mRNA of each one of this plurality of VGAM1398 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1398 RNA, herein designated VGAM RNA, and which when bound by VGAM1398 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1398 host target proteins.

[19536] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1398 gene, herein designated VGAM GENE, on one or more VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,



Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [19537] It is yet further appreciated that a function of VGAM1398 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of viral infection by Caprine arthritis–en–cephalitis virus. Specific functions, and accordingly utilities, of VGAM1398 correlate with, and may be deduced from, the identity of the host target genes which VGAM1398 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [19538] Nucleotide sequences of the VGAM1398 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1398 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1398 are further described hereinbelow with reference to Table 1.
- [19539] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1398 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19540] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1399 (VGAM1399) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19541] VGAM1399 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1399 was detected is described hereinabove with reference to Figs. 2-8.

[19542] VGAM1399 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Caprine arthritis-encephalitis virus. VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19543] VGAM1399 gene, herein designated VGAM GENE, encodes a VGAM1399 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1399 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1399 precursor RNA is designated SEQ ID:35877, and is provided hereinbelow with reference to the sequence listing part.

[19544] VGAM1399 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19545] An enzyme complex designated DICER COMPLEX, dices the VGAM1399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1399 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1399 RNA is designated SEQ ID:35878, and is provided hereinbelow with reference to the sequence listing part.

[19546] VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19547] VGAM1399 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1399 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1399 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19548] The complementary binding of VGAM1399 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1399 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19549] It is appreciated that VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1399 host target genes. The mRNA of

each one of this plurality of VGAM1399 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1399 RNA, herein designated VGAM RNA, and which when bound by VGAM1399 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1399 host target proteins.

[19550] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1399 gene, herein designated VGAM GENE, on one or more VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[19551] It is yet further appreciated that a function of VGAM1399 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1399 include diagnosis, prevention and treatment of viral infection by Caprine arthritis–encephalitis virus. Specific functions, and accordingly utilities, of VGAM1399 correlate with, and may be deduced from, the identity of the host target genes which VGAM1399 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19552] Nucleotide sequences of the VGAM1399 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1399 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1399 are further described hereinbelow with reference to Table 1.

[19553] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1399 RNA, herein designated VGAM RNA, are de–

scribed hereinbelow with reference to Table 2.

[19554] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1400 (VGAM1400) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19555] VGAM1400 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1400 was detected is described hereinabove with reference to Figs. 2–8.

[19556] VGAM1400 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cardamine chlorotic fleck virus. VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19557] VGAM1400 gene, herein designated VGAM GENE, encodes a VGAM1400 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1400 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly



similar to the nucleotide sequence of VGAM1400 precursor RNA is designated SEQ ID:35889, and is provided hereinbelow with reference to the sequence listing part.

[19558] VGAM1400 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1400 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19559] An enzyme complex designated DICER COMPLEX, dices the VGAM1400 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1400 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1400 RNA is designated SEQ ID:35890,

and is provided hereinbelow with reference to the sequence listing part.

[19560] VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19561] VGAM1400 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1400 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1400 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19562] The complementary binding of VGAM1400 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1400 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19563] It is appreciated that VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1400 host target genes. The mRNA of each one of this plurality of VGAM1400 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1400 RNA, herein designated VGAM RNA, and which when bound by VGAM1400 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1400 host target proteins.

[19564] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1400 gene, herein designated VGAM GENE, on one or more VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19565] It is yet further appreciated that a function of VGAM1400 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1400 include diagnosis, prevention and treatment of viral infection by Cardamine chlorotic fleck virus. Specific functions, and accordingly utilities, of VGAM1400 correlate with, and may be deduced from, the identity of the host target genes which VGAM1400 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19566] Nucleotide sequences of the VGAM1400 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1400 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1400 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1400 are further described hereinbelow with reference to Table 1.

[19567] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1400 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19568] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1401 (VGAM1401) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19569] VGAM1401 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1401 was detected is described hereinabove with reference to Figs. 2–8.

[19570] VGAM1401 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19571] VGAM1401 gene, herein designated VGAM GENE, encodes a VGAM1401 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1401 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1401 precu-

sor RNA is designated SEQ ID:35926, and is provided hereinbelow with reference to the sequence listing part.

[19572] VGAM1401 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19573] An enzyme complex designated DICER COMPLEX, dices the VGAM1401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1401 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1401 RNA is designated SEQ ID:35927, and is provided hereinbelow with reference to the se-

quence listing part.

[19574] VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19575] VGAM1401 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not



meant to be limiting VGAM1401 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19576] The complementary binding of VGAM1401 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1401 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19577] It is appreciated that VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1401 host target genes. The mRNA of each one of this plurality of VGAM1401 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1401 RNA, herein designated VGAM RNA, and which when bound by VGAM1401 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1401 host target proteins.

[19578] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1401 gene, herein designated VGAM GENE, on one or more VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19579] It is yet further appreciated that a function of VGAM1401

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1401 correlate with, and may be deduced from, the identity of the host target genes which VGAM1401 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19580] Nucleotide sequences of the VGAM1401 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1401 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1401 are further described hereinbelow with reference to Table 1.

[19581] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1401 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19582] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1402 (VGAM1402) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19583] VGAM1402 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1402 was detected is described hereinabove with reference to Figs. 2–8.

[19584] VGAM1402 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19585] VGAM1402 gene, herein designated VGAM GENE, encodes a VGAM1402 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1402 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1402 precursor RNA is designated SEQ ID:35933, and is provided

hereinbelow with reference to the sequence listing part.

[19586] VGAM1402 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1402 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19587] An enzyme complex designated DICER COMPLEX, dices the VGAM1402 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1402 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1402 RNA is designated SEQ ID:35934, and is provided hereinbelow with reference to the sequence listing part.

[19588] VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19589] VGAM1402 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1402 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1402 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19590] The complementary binding of VGAM1402 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1402 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19591] It is appreciated that VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1402 host target genes. The mRNA of each one of this plurality of VGAM1402 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1402 RNA, herein designated VGAM RNA, and which when bound by VGAM1402 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1402 host target proteins.

[19592] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1402 gene, herein designated VGAM GENE, on one or more VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19593] It is yet further appreciated that a function of VGAM1402 is inhibition of expression of host target genes, as part of



a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1402 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1402 correlate with, and may be deduced from, the identity of the host target genes which VGAM1402 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19594] Nucleotide sequences of the VGAM1402 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1402 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1402 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1402 are further described hereinbelow with reference to Table 1.

[19595] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1402 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19596] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1403 (VGAM1403) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19597] VGAM1403 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1403 was detected is described hereinabove with reference to Figs. 2–8.

[19598] VGAM1403 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1403 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19599] VGAM1403 gene, herein designated VGAM GENE, encodes a VGAM1403 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1403 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1403 precursor RNA is designated SEQ ID:35968, and is provided hereinbelow with reference to the sequence listing part.

[19600] VGAM1403 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19601] An enzyme complex designated DICER COMPLEX, dices the VGAM1403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1403 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1403 RNA is designated SEQ ID:35969, and is provided hereinbelow with reference to the sequence listing part.

[19602] VGAM1403 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19603] VGAM1403 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1403 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19604] The complementary binding of VGAM1403 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1403 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19605] It is appreciated that VGAM1403 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1403 host target genes. The mRNA of each one of this plurality of VGAM1403 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1403 RNA, herein designated VGAM

RNA, and which when bound by VGAM1403 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1403 host target proteins.

[19606] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1403 gene, herein designated VGAM GENE, on one or more VGAM1403 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19607] It is yet further appreciated that a function of VGAM1403 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1403 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1403 correlate with, and may be deduced from, the identity of the host target genes which VGAM1403 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19608] Nucleotide sequences of the VGAM1403 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1403 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1403 are further described hereinbelow with reference to Table 1.

[19609] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1403 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19610] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1404 (VGAM1404) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19611] VGAM1404 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1404 was detected is described hereinabove with reference to Figs. 2-8.

[19612] VGAM1404 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cardamine chlorotic fleck virus. VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19613] VGAM1404 gene, herein designated VGAM GENE, encodes a VGAM1404 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1404 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1404 precursor RNA is designated SEQ ID:35990, and is provided hereinbelow with reference to the sequence listing part.

[19614] VGAM1404 precursor RNA, herein designated VGAM PRE-



CURSOR RNA, folds onto itself, forming VGAM1404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19615] An enzyme complex designated DICER COMPLEX, dices the VGAM1404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1404 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1404 RNA is designated SEQ ID:35991, and is provided hereinbelow with reference to the sequence listing part.

[19616] VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19617] VGAM1404 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1404 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1404 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1404 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19618] The complementary binding of VGAM1404 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1404 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19619] It is appreciated that VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1404 host target genes. The mRNA of each one of this plurality of VGAM1404 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1404 RNA, herein designated VGAM RNA, and which when bound by VGAM1404 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1404 host target proteins.

[19620] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1404 gene, herein designated VGAM GENE, on one or more VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19621] It is yet further appreciated that a function of VGAM1404 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1404 include diagnosis, prevention and

treatment of viral infection by Cardamine chlorotic fleck virus. Specific functions, and accordingly utilities, of VGAM1404 correlate with, and may be deduced from, the identity of the host target genes which VGAM1404 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19622] Nucleotide sequences of the VGAM1404 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1404 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1404 are further described hereinbelow with reference to Table 1.

[19623] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1404 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19624] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1405 (VGAM1405) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19625] VGAM1405 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1405 was detected is described hereinabove with reference to Figs. 2–8.

[19626] VGAM1405 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19627] VGAM1405 gene, herein designated VGAM GENE, encodes a VGAM1405 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1405 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1405 precursor RNA is designated SEQ ID:36006, and is provided hereinbelow with reference to the sequence listing part.

[19628] VGAM1405 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1405 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19629] An enzyme complex designated DICER COMPLEX, dices the VGAM1405 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1405 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1405 RNA is designated SEQ ID:36007, and is provided hereinbelow with reference to the sequence listing part.

[19630] VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1405 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19631] VGAM1405 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1405 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA.



It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19632] The complementary binding of VGAM1405 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1405 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19633] It is appreciated that VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1405 host target genes. The mRNA of each one of this plurality of VGAM1405 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1405 RNA, herein designated VGAM RNA, and which when bound by VGAM1405 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1405 host target proteins.

[19634] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1405 gene, herein designated VGAM GENE, on one or more VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19635] It is yet further appreciated that a function of VGAM1405 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Spe-

cific functions, and accordingly utilities, of VGAM1405 correlate with, and may be deduced from, the identity of the host target genes which VGAM1405 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19636] Nucleotide sequences of the VGAM1405 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1405 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1405 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1405 are further described hereinbelow with reference to Table 1.

[19637] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1405 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19638] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1406 (VGAM1406) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[19639] VGAM1406 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1406 was detected is described hereinabove with reference to Figs. 2–8.

[19640] VGAM1406 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19641] VGAM1406 gene, herein designated VGAM GENE, encodes a VGAM1406 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1406 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1406 precursor RNA is designated SEQ ID:36022, and is provided hereinbelow with reference to the sequence listing part.

[19642] VGAM1406 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1406 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19643] An enzyme complex designated DICER COMPLEX, dices the VGAM1406 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1406 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1406 RNA is designated SEQ ID:36023, and is provided hereinbelow with reference to the sequence listing part.

[19644] VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1406 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19645] VGAM1406 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1406 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1406 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19646] The complementary binding of VGAM1406 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1406 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19647] It is appreciated that VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1406 host target genes. The mRNA of each one of this plurality of VGAM1406 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1406 RNA, herein designated VGAM RNA, and which when bound by VGAM1406 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1406 host target proteins.

[19648] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1406 gene, herein designated VGAM GENE, on one or more VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19649] It is yet further appreciated that a function of VGAM1406 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1406 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1406



correlate with, and may be deduced from, the identity of the host target genes which VGAM1406 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19650] Nucleotide sequences of the VGAM1406 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1406 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1406 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1406 are further described hereinbelow with reference to Table 1.

[19651] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1406 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19652] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1407 (VGAM1407) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[19653] VGAM1407 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1407 was detected is described hereinabove with reference to Figs. 2–8.

[19654] VGAM1407 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine herpesvirus 1. VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19655] VGAM1407 gene, herein designated VGAM GENE, encodes a VGAM1407 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1407 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1407 precursor RNA is designated SEQ ID:36062, and is provided hereinbelow with reference to the sequence listing part.

[19656] VGAM1407 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19657] An enzyme complex designated DICER COMPLEX, dices the VGAM1407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1407 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1407 RNA is designated SEQ ID:36063, and is provided hereinbelow with reference to the sequence listing part.

[19658] VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19659] VGAM1407 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1407 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19660] The complementary binding of VGAM1407 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1407 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19661] It is appreciated that VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1407 host target genes. The mRNA of each one of this plurality of VGAM1407 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1407 RNA, herein designated VGAM RNA, and which when bound by VGAM1407 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1407 host target proteins.

[19662] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1407 gene, herein designated VGAM GENE, on one or more VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19663] It is yet further appreciated that a function of VGAM1407 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of viral infection by Equine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1407 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1407 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19664] Nucleotide sequences of the VGAM1407 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1407 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1407 are further described hereinbelow with reference to Table 1.

[19665] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1407 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19666] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1408 (VGAM1408) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19667] VGAM1408 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1408 was detected is described hereinabove with reference to Figs. 2–8.

[19668] VGAM1408 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine herpesvirus 1. VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19669] VGAM1408 gene, herein designated VGAM GENE, encodes a VGAM1408 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1408 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1408 precursor RNA is designated SEQ ID:36085, and is provided hereinbelow with reference to the sequence listing part.

[19670] VGAM1408 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-



cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19671] An enzyme complex designated DICER COMPLEX, dices the VGAM1408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1408 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1408 RNA is designated SEQ ID:36086, and is provided hereinbelow with reference to the sequence listing part.

[19672] VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19673] VGAM1408 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1408 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1408 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19674] The complementary binding of VGAM1408 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1408 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19675] It is appreciated that VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1408 host target genes. The mRNA of each one of this plurality of VGAM1408 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1408 RNA, herein designated VGAM RNA, and which when bound by VGAM1408 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1408 host target proteins.

[19676] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1408 gene, herein designated VGAM GENE, on one or more VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19677] It is yet further appreciated that a function of VGAM1408 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1408 include diagnosis, prevention and treatment of viral infection by Bovine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1408 correlate with, and may be deduced from, the identity of the host target genes which VGAM1408 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[19678] Nucleotide sequences of the VGAM1408 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1408 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1408 are further described hereinbelow with reference to Table 1.

[19679] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1408 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19680] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1409 (VGAM1409) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19681] VGAM1409 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1409 was detected is described hereinabove with reference to Figs. 2–8.

[19682] VGAM1409 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1409 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19683] VGAM1409 gene, herein designated VGAM GENE, encodes a VGAM1409 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1409 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1409 precursor RNA is designated SEQ ID:36091, and is provided hereinbelow with reference to the sequence listing part.

[19684] VGAM1409 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1409 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19685] An enzyme complex designated DICER COMPLEX, dices the VGAM1409 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1409 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1409 RNA is designated SEQ ID:36092, and is provided hereinbelow with reference to the sequence listing part.

[19686] VGAM1409 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19687] VGAM1409 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1409 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both



3UTR and 5UTR regions.

[19688] The complementary binding of VGAM1409 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1409 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19689] It is appreciated that VGAM1409 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1409 host target genes. The mRNA of each one of this plurality of VGAM1409 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1409 RNA, herein designated VGAM RNA, and which when bound by VGAM1409 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1409 host target proteins.

[19690] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1409 gene, herein designated VGAM GENE, on one or more VGAM1409 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19691] It is yet further appreciated that a function of VGAM1409 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1409 correlate with, and may be deduced from, the identity of the host target genes which VGAM1409 binds and inhibits, and the function of these host target

genes, as elaborated hereinbelow.

[19692] Nucleotide sequences of the VGAM1409 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1409 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1409 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1409 are further described hereinbelow with reference to Table 1.

[19693] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1409 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19694] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1410 (VGAM1410) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19695] VGAM1410 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1410 was detected is described hereinabove with reference to Figs. 2–8.

[19696] VGAM1410 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Rana tigrina* ranavirus. VGAM1410 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19697] VGAM1410 gene, herein designated VGAM GENE, encodes a VGAM1410 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1410 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1410 precursor RNA is designated SEQ ID:36094, and is provided hereinbelow with reference to the sequence listing part.

[19698] VGAM1410 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19699] An enzyme complex designated DICER COMPLEX, dices the VGAM1410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1410 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1410 RNA is designated SEQ ID:36095, and is provided hereinbelow with reference to the sequence listing part.

[19700] VGAM1410 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[19701] VGAM1410 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1410 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19702] The complementary binding of VGAM1410 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1410 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19703] It is appreciated that VGAM1410 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1410 host target genes. The mRNA of each one of this plurality of VGAM1410 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1410 RNA, herein designated VGAM RNA, and which when bound by VGAM1410 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1410 host target proteins.

[19704] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1410 gene, herein designated VGAM GENE, on one

or more VGAM1410 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19705] It is yet further appreciated that a function of VGAM1410 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM1410 correlate with, and may be deduced from, the identity of the host target genes which VGAM1410 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.



[19706] Nucleotide sequences of the VGAM1410 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1410 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1410 are further described hereinbelow with reference to Table 1.

[19707] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1410 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19708] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1411 (VGAM1411) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19709] VGAM1411 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1411 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[19710] VGAM1411 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM1411 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19711] VGAM1411 gene, herein designated VGAM GENE, encodes a VGAM1411 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1411 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1411 precursor RNA is designated SEQ ID:36101, and is provided hereinbelow with reference to the sequence listing part.

[19712] VGAM1411 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19713] An enzyme complex designated DICER COMPLEX, dices the VGAM1411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1411 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1411 RNA is designated SEQ ID:36102, and is provided hereinbelow with reference to the sequence listing part.

[19714] VGAM1411 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19715] VGAM1411 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1411 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1411 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19716] The complementary binding of VGAM1411 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1411 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19717] It is appreciated that VGAM1411 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1411 host target genes. The mRNA of each one of this plurality of VGAM1411 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1411 RNA, herein designated VGAM RNA, and which when bound by VGAM1411 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1411 host target proteins.

[19718] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1411 gene, herein designated VGAM GENE, on one or more VGAM1411 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19719] It is yet further appreciated that a function of VGAM1411 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1411 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM1411 correlate with, and may be deduced from, the identity of the host target genes which VGAM1411 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19720] Nucleotide sequences of the VGAM1411 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1411 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1411 are further described hereinbelow with reference to Table 1.

[19721] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1411 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19722] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1412 (VGAM1412) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19723] VGAM1412 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1412 was detected is described hereinabove with reference to Figs. 2-8.

[19724] VGAM1412 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19725] VGAM1412 gene, herein designated VGAM GENE, encodes a VGAM1412 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1412 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1412 precursor RNA is designated SEQ ID:36117, and is provided hereinbelow with reference to the sequence listing part.

[19726] VGAM1412 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of



the second half thereof.

[19727] An enzyme complex designated DICER COMPLEX, dices the VGAM1412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1412 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1412 RNA is designated SEQ ID:36118, and is provided hereinbelow with reference to the sequence listing part.

[19728] VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19729] VGAM1412 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1412 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1412 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19730] The complementary binding of VGAM1412 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1412 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19731] It is appreciated that VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1412 host target genes. The mRNA of each one of this plurality of VGAM1412 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1412 RNA, herein designated VGAM RNA, and which when bound by VGAM1412 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1412 host target proteins.

[19732] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1412 gene, herein designated VGAM GENE, on one or more VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19733] It is yet further appreciated that a function of VGAM1412 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1412 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM1412 correlate with, and may be deduced from, the identity of the host target genes which VGAM1412 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19734] Nucleotide sequences of the VGAM1412 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1412 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1412 are further described hereinbelow with reference to Table 1.

[19735] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1412 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19736] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1413 (VGAM1413) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19737] VGAM1413 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1413 was detected is described hereinabove with reference to Figs. 2-8.

[19738] VGAM1413 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Gallid herpesvirus 2. VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19739] VGAM1413 gene, herein designated VGAM GENE, encodes a VGAM1413 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1413 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1413 precursor RNA is designated SEQ ID:36131, and is provided hereinbelow with reference to the sequence listing part.

[19740] VGAM1413 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1413 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19741] An enzyme complex designated DICER COMPLEX, dices the VGAM1413 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1413 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1413 RNA is designated SEQ ID:36132, and is provided hereinbelow with reference to the sequence listing part.

[19742] VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19743] VGAM1413 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1413 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19744] The complementary binding of VGAM1413 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1413 host target RNA, herein designated VGAM



HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1413 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19745] It is appreciated that VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1413 host target genes. The mRNA of each one of this plurality of VGAM1413 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1413 RNA, herein designated VGAM RNA, and which when bound by VGAM1413 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1413 host target proteins.

[19746] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1413 gene, herein designated VGAM GENE, on one or more VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19747] It is yet further appreciated that a function of VGAM1413 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of viral infection by Gallid herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1413 correlate with, and may be deduced from, the identity of the host target genes which VGAM1413 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19748] Nucleotide sequences of the VGAM1413 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1413 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1413 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1413 are further described hereinbelow with reference to Table 1.

[19749] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1413 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19750] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1414 (VGAM1414) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19751] VGAM1414 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1414 was detected is described hereinabove with reference to Figs. 2-8.

[19752] VGAM1414 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus.

VGAM1414 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19753] VGAM1414 gene, herein designated VGAM GENE, encodes a VGAM1414 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1414 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1414 precursor RNA is designated SEQ ID:36163, and is provided hereinbelow with reference to the sequence listing part.

[19754] VGAM1414 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1414 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19755] An enzyme complex designated DICER COMPLEX, dices

the VGAM1414 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1414 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1414 RNA is designated SEQ ID:36164, and is provided hereinbelow with reference to the sequence listing part.

[19756] VGAM1414 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19757] VGAM1414 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1414 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1414 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1414 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19758] The complementary binding of VGAM1414 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1414 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19759] It is appreciated that VGAM1414 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1414 host target genes. The mRNA of each one of this plurality of VGAM1414 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1414 RNA, herein designated VGAM RNA, and which when bound by VGAM1414 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1414 host target proteins.

[19760] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1414 gene, herein designated VGAM GENE, on one or more VGAM1414 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19761] It is yet further appreciated that a function of VGAM1414 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1414 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM1414 correlate with, and may be deduced from, the identity of the host target genes which VGAM1414 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19762] Nucleotide sequences of the VGAM1414 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1414 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM1414 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1414 are further described hereinbelow with reference to Table 1.

[19763] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1414 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19764] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1415 (VGAM1415) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19765] VGAM1415 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1415 was detected is described hereinabove with reference to Figs. 2-8.

[19766] VGAM1415 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus sanguinipes entomopoxvirus. VGAM1415 host target gene, herein

designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19767] VGAM1415 gene, herein designated VGAM GENE, encodes a VGAM1415 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1415 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1415 precursor RNA is designated SEQ ID:36180, and is provided hereinbelow with reference to the sequence listing part.

[19768] VGAM1415 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1415 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19769] An enzyme complex designated DICER COMPLEX, dices the VGAM1415 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1415 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1415 RNA is designated SEQ ID:36181, and is provided hereinbelow with reference to the sequence listing part.

[19770] VGAM1415 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19771] VGAM1415 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1415 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1415 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19772] The complementary binding of VGAM1415 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1415

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1415 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19773] It is appreciated that VGAM1415 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1415 host target genes. The mRNA of each one of this plurality of VGAM1415 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1415 RNA, herein designated VGAM RNA, and which when bound by VGAM1415 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1415 host target proteins.

[19774] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1415 gene, herein designated VGAM GENE, on one or more VGAM1415 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19775] It is yet further appreciated that a function of VGAM1415 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1415 include diagnosis, prevention and treatment of viral infection by Melanoplus sanguinipes entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1415 correlate with, and may be deduced from, the identity of the host target genes which VGAM1415 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19776] Nucleotide sequences of the VGAM1415 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1415 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1415 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1415 are further described hereinbelow with reference to Table 1.

[19777] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1415 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19778] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1416 (VGAM1416) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19779] VGAM1416 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1416 was detected is described hereinabove with reference to Figs. 2-8.

[19780] VGAM1416 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[19781] VGAM1416 gene, herein designated VGAM GENE, encodes a VGAM1416 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1416 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1416 precursor RNA is designated SEQ ID:36183, and is provided hereinbelow with reference to the sequence listing part.

[19782] VGAM1416 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19783] An enzyme complex designated DICER COMPLEX, dices the VGAM1416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1416 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1416 RNA is designated SEQ ID:36184, and is provided hereinbelow with reference to the sequence listing part.

[19784] VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19785] VGAM1416 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1416 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1416 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19786] The complementary binding of VGAM1416 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1416 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1416 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19787] It is appreciated that VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1416 host target genes. The mRNA of each one of this plurality of VGAM1416 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1416 RNA, herein designated VGAM RNA, and which when bound by VGAM1416 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1416 host target proteins.

[19788] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1416 gene, herein designated VGAM GENE, on one or more VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19789] It is yet further appreciated that a function of VGAM1416 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1416 include diagnosis, prevention and treatment of viral infection by Rana tigrina ranavirus. Specific functions, and accordingly utilities, of VGAM1416 correlate with, and may be deduced from, the identity of the host target genes which VGAM1416 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19790] Nucleotide sequences of the VGAM1416 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1416 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1416 are further

described hereinbelow with reference to Table 1.

[19791] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1416 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19792] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1417 (VGAM1417) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19793] VGAM1417 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1417 was detected is described hereinabove with reference to Figs. 2-8.

[19794] VGAM1417 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1417 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19795] VGAM1417 gene, herein designated VGAM GENE, encodes a VGAM1417 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1417 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1417 precursor RNA is designated SEQ ID:36204, and is provided hereinbelow with reference to the sequence listing part.

[19796] VGAM1417 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1417 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19797] An enzyme complex designated DICER COMPLEX, dices the VGAM1417 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1417 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1417 RNA is designated SEQ ID:36205, and is provided hereinbelow with reference to the sequence listing part.

[19798] VGAM1417 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1417 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1417 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19799] VGAM1417 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1417 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1417 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1417 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1417 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19800] The complementary binding of VGAM1417 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1417 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1417 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1417 host target protein, herein desig-



nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19801] It is appreciated that VGAM1417 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1417 host target genes. The mRNA of each one of this plurality of VGAM1417 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1417 RNA, herein designated VGAM RNA, and which when bound by VGAM1417 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1417 host target proteins.

[19802] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1417 gene, herein designated VGAM GENE, on one or more VGAM1417 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19803] It is yet further appreciated that a function of VGAM1417 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1417 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1417 correlate with, and may be deduced from, the identity of the host target genes which VGAM1417 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19804] Nucleotide sequences of the VGAM1417 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1417 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1417 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1417 are further described hereinbelow with reference to Table 1.

[19805] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1417 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19806] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1418 (VGAM1418) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19807] VGAM1418 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1418 was detected is described hereinabove with reference to Figs. 2-8.

[19808] VGAM1418 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 6B. VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19809] VGAM1418 gene, herein designated VGAM GENE, encodes

a VGAM1418 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1418 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1418 precursor RNA is designated SEQ ID:36214, and is provided hereinbelow with reference to the sequence listing part.

[19810] VGAM1418 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19811] An enzyme complex designated DICER COMPLEX, dices the VGAM1418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1418 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1418 RNA is designated SEQ ID:36215, and is provided hereinbelow with reference to the sequence listing part.

[19812] VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19813] VGAM1418 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1418 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1418 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19814] The complementary binding of VGAM1418 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1418 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[19815] It is appreciated that VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1418 host target genes. The mRNA of each one of this plurality of VGAM1418 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1418 RNA, herein designated VGAM RNA, and which when bound by VGAM1418 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1418 host target proteins.

[19816] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1418 gene, herein designated VGAM GENE, on one or more VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19817] It is yet further appreciated that a function of VGAM1418 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1418 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 6B. Specific functions, and accordingly utilities, of VGAM1418 correlate with, and may be deduced from, the identity of the host target genes which VGAM1418 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19818] Nucleotide sequences of the VGAM1418 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1418 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1418 are further described hereinbelow with reference to Table 1.

[19819] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1418 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19820] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1419 (VGAM1419) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19821] VGAM1419 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1419 was detected is described hereinabove with reference to Figs. 2-8.

[19822] VGAM1419 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19823] VGAM1419 gene, herein designated VGAM GENE, encodes a VGAM1419 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1419 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1419 precursor RNA is designated SEQ ID:36217, and is provided hereinbelow with reference to the sequence listing part.

[19824] VGAM1419 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1419 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19825] An enzyme complex designated DICER COMPLEX, dices the VGAM1419 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1419 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1419 RNA is designated SEQ ID:36218, and is provided hereinbelow with reference to the sequence listing part.

[19826] VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19827] VGAM1419 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1419 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19828] The complementary binding of VGAM1419 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1419 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19829] It is appreciated that VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1419 host target genes. The mRNA of each one of this plurality of VGAM1419 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1419 RNA, herein designated VGAM RNA, and which when bound by VGAM1419 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1419 host target proteins.

[19830] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1419 gene, herein designated VGAM GENE, on one or more VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19831] It is yet further appreciated that a function of VGAM1419 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1419 correlate with, and may be deduced from, the identity of the host target genes which VGAM1419 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19832] Nucleotide sequences of the VGAM1419 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1419 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1419 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1419 are further described hereinbelow with reference to Table 1.

[19833] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1419 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19834] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1420 (VGAM1420) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19835] VGAM1420 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1420 was detected is described hereinabove with reference to Figs. 2-8.

[19836] VGAM1420 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1420 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19837] VGAM1420 gene, herein designated VGAM GENE, encodes a VGAM1420 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1420 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1420 precursor RNA is designated SEQ ID:36220, and is provided hereinbelow with reference to the sequence listing part.

[19838] VGAM1420 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19839] An enzyme complex designated DICER COMPLEX, dices the VGAM1420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1420 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1420 RNA is designated SEQ ID:36221, and is provided hereinbelow with reference to the sequence listing part.

[19840] VGAM1420 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19841] VGAM1420 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1420 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19842] The complementary binding of VGAM1420 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1420 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19843] It is appreciated that VGAM1420 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1420 host target genes. The mRNA of each one of this plurality of VGAM1420 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1420 RNA, herein designated VGAM RNA, and which when bound by VGAM1420 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1420 host target proteins.

[19844] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1420 gene, herein designated VGAM GENE, on one or more VGAM1420 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19845] It is yet further appreciated that a function of VGAM1420 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1420 correlate with, and may be deduced from, the identity of the host target genes which VGAM1420 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19846] Nucleotide sequences of the VGAM1420 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1420 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1420 are further described hereinbelow with reference to Table 1.

[19847] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1420 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19848] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1421 (VGAM1421) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19849] VGAM1421 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1421 was detected is described hereinabove with reference to Figs. 2–8.

[19850] VGAM1421 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19851] VGAM1421 gene, herein designated VGAM GENE, encodes a VGAM1421 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1421 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1421 precursor RNA is designated SEQ ID:36240, and is provided hereinbelow with reference to the sequence listing part.

[19852] VGAM1421 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19853] An enzyme complex designated DICER COMPLEX, dices the VGAM1421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1421 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1421 RNA is designated SEQ ID:36241, and is provided hereinbelow with reference to the sequence listing part.

[19854] VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19855] VGAM1421 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1421 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19856] The complementary binding of VGAM1421 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1421 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19857] It is appreciated that VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1421 host target genes. The mRNA of each one of this plurality of VGAM1421 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1421 RNA, herein designated VGAM RNA, and which when bound by VGAM1421 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1421 host target proteins.

[19858] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1421 gene, herein designated VGAM GENE, on one or more VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [19859] It is yet further appreciated that a function of VGAM1421 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1421 correlate with, and may be deduced from, the identity of the host target genes which VGAM1421 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [19860] Nucleotide sequences of the VGAM1421 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1421 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1421 are further described hereinbelow with reference to Table 1.
- [19861] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1421 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19862] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1422 (VGAM1422) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19863] VGAM1422 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1422 was detected is described hereinabove with reference to Figs. 2-8.

[19864] VGAM1422 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy skin disease virus. VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19865] VGAM1422 gene, herein designated VGAM GENE, encodes a VGAM1422 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1422 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1422 precursor RNA is designated SEQ ID:36257, and is provided hereinbelow with reference to the sequence listing part.

[19866] VGAM1422 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19867] An enzyme complex designated DICER COMPLEX, dices the VGAM1422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1422 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM1422 RNA is designated SEQ ID:35745, and is provided hereinbelow with reference to the sequence listing part.

[19868] VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19869] VGAM1422 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1422 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19870] The complementary binding of VGAM1422 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1422 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19871] It is appreciated that VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1422 host target genes. The mRNA of

each one of this plurality of VGAM1422 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1422 RNA, herein designated VGAM RNA, and which when bound by VGAM1422 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1422 host target proteins.

[19872] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1422 gene, herein designated VGAM GENE, on one or more VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[19873] It is yet further appreciated that a function of VGAM1422 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of viral infection by Lumpy skin disease virus. Specific functions, and accordingly utilities, of VGAM1422 correlate with, and may be deduced from, the identity of the host target genes which VGAM1422 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19874] Nucleotide sequences of the VGAM1422 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1422 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1422 are further described hereinbelow with reference to Table 1.

[19875] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1422 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[19876] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1423 (VGAM1423) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19877] VGAM1423 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1423 was detected is described hereinabove with reference to Figs. 2–8.

[19878] VGAM1423 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19879] VGAM1423 gene, herein designated VGAM GENE, encodes a VGAM1423 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1423 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1423 precursor RNA is designated SEQ ID:36258, and is provided hereinbelow with reference to the sequence listing part.

[19880] VGAM1423 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1423 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19881] An enzyme complex designated DICER COMPLEX, dices the VGAM1423 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1423 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1423 RNA is designated SEQ ID:36259,

and is provided hereinbelow with reference to the sequence listing part.

[19882] VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19883] VGAM1423 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1423 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19884] The complementary binding of VGAM1423 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1423 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19885] It is appreciated that VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1423 host target genes. The mRNA of each one of this plurality of VGAM1423 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1423 RNA, herein designated VGAM RNA, and which when bound by VGAM1423 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1423 host target proteins.

[19886] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1423 gene, herein designated VGAM GENE, on one or more VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19887] It is yet further appreciated that a function of VGAM1423 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1423 correlate with, and may be deduced from, the identity of the host target genes which VGAM1423 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19888] Nucleotide sequences of the VGAM1423 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1423 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1423 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1423 are further described hereinbelow with reference to Table 1.

[19889] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1423 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19890] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1424 (VGAM1424) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19891] VGAM1424 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1424 was detected is described hereinabove with reference to Figs. 2–8.

[19892] VGAM1424 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19893] VGAM1424 gene, herein designated VGAM GENE, encodes a VGAM1424 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1424 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1424 precu-

sor RNA is designated SEQ ID:36291, and is provided hereinbelow with reference to the sequence listing part.

[19894] VGAM1424 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19895] An enzyme complex designated DICER COMPLEX, dices the VGAM1424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1424 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1424 RNA is designated SEQ ID:36292, and is provided hereinbelow with reference to the se-



quence listing part.

[19896] VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19897] VGAM1424 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1424 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1424 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19898] The complementary binding of VGAM1424 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1424 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19899] It is appreciated that VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1424 host target genes. The mRNA of each one of this plurality of VGAM1424 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1424 RNA, herein designated VGAM RNA, and which when bound by VGAM1424 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1424 host target proteins.

[19900] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1424 gene, herein designated VGAM GENE, on one or more VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19901] It is yet further appreciated that a function of VGAM1424

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1424 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1424 correlate with, and may be deduced from, the identity of the host target genes which VGAM1424 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19902] Nucleotide sequences of the VGAM1424 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1424 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1424 are further described hereinbelow with reference to Table 1.

[19903] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1424 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19904] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1425 (VGAM1425) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19905] VGAM1425 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1425 was detected is described hereinabove with reference to Figs. 2–8.

[19906] VGAM1425 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus E. VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19907] VGAM1425 gene, herein designated VGAM GENE, encodes a VGAM1425 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1425 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1425 precursor RNA is designated SEQ ID:36300, and is provided

hereinbelow with reference to the sequence listing part.

[19908] VGAM1425 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19909] An enzyme complex designated DICER COMPLEX, dices the VGAM1425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1425 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1425 RNA is designated SEQ ID:36301, and is provided hereinbelow with reference to the sequence listing part.

[19910] VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19911] VGAM1425 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1425 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1425 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19912] The complementary binding of VGAM1425 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1425 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19913] It is appreciated that VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1425 host target genes. The mRNA of each one of this plurality of VGAM1425 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM1425 RNA, herein designated VGAM RNA, and which when bound by VGAM1425 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1425 host target proteins.

[19914] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1425 gene, herein designated VGAM GENE, on one or more VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19915] It is yet further appreciated that a function of VGAM1425 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1425 include diagnosis, prevention and treatment of viral infection by Human adenovirus E. Specific functions, and accordingly utilities, of VGAM1425 correlate with, and may be deduced from, the identity of the host target genes which VGAM1425 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19916] Nucleotide sequences of the VGAM1425 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1425 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1425 are further described hereinbelow with reference to Table 1.

[19917] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1425 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19918] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1426 (VGAM1426) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19919] VGAM1426 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1426 was detected is described hereinabove with reference to Figs. 2–8.

[19920] VGAM1426 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Japanese iris necrotic ring virus. VGAM1426 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19921] VGAM1426 gene, herein designated VGAM GENE, encodes a VGAM1426 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1426 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1426 precursor RNA is designated SEQ ID:36320, and is provided hereinbelow with reference to the sequence listing part.

[19922] VGAM1426 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19923] An enzyme complex designated DICER COMPLEX, dices the VGAM1426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1426 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1426 RNA is designated SEQ ID:36321, and is provided hereinbelow with reference to the sequence listing part.

[19924] VGAM1426 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19925] VGAM1426 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1426 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1426 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19926] The complementary binding of VGAM1426 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1426 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19927] It is appreciated that VGAM1426 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1426 host target genes. The mRNA of each one of this plurality of VGAM1426 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1426 RNA, herein designated VGAM

RNA, and which when bound by VGAM1426 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1426 host target proteins.

[19928] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1426 gene, herein designated VGAM GENE, on one or more VGAM1426 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19929] It is yet further appreciated that a function of VGAM1426 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1426 include diagnosis, prevention and treatment of viral infection by Japanese iris necrotic ring virus. Specific functions, and accordingly utilities, of VGAM1426 correlate with, and may be deduced from, the identity of the host target genes which VGAM1426 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19930] Nucleotide sequences of the VGAM1426 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1426 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1426 are further described hereinbelow with reference to Table 1.

[19931] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1426 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19932] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 1427 (VGAM1427) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19933] VGAM1427 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1427 was detected is described hereinabove with reference to Figs. 2-8.

[19934] VGAM1427 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Japanese iris necrotic ring virus. VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19935] VGAM1427 gene, herein designated VGAM GENE, encodes a VGAM1427 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1427 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1427 precursor RNA is designated SEQ ID:36346, and is provided hereinbelow with reference to the sequence listing part.

[19936] VGAM1427 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19937] An enzyme complex designated DICER COMPLEX, dices the VGAM1427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1427 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1427 RNA is designated SEQ ID:36347, and is provided hereinbelow with reference to the sequence listing part.

[19938] VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19939] VGAM1427 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1427 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1427 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19940] The complementary binding of VGAM1427 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1427 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19941] It is appreciated that VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1427 host target genes. The mRNA of each one of this plurality of VGAM1427 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1427 RNA, herein designated VGAM RNA, and which when bound by VGAM1427 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1427 host target proteins.

[19942] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1427 gene, herein designated VGAM GENE, on one or more VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19943] It is yet further appreciated that a function of VGAM1427 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1427 include diagnosis, prevention and

treatment of viral infection by Japanese iris necrotic ring virus. Specific functions, and accordingly utilities, of VGAM1427 correlate with, and may be deduced from, the identity of the host target genes which VGAM1427 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19944] Nucleotide sequences of the VGAM1427 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1427 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1427 are further described hereinbelow with reference to Table 1.

[19945] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1427 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19946] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1428 (VGAM1428) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[19947] VGAM1428 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1428 was detected is described hereinabove with reference to Figs. 2–8.

[19948] VGAM1428 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19949] VGAM1428 gene, herein designated VGAM GENE, encodes a VGAM1428 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1428 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1428 precursor RNA is designated SEQ ID:36357, and is provided hereinbelow with reference to the sequence listing part.

[19950] VGAM1428 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1428 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19951] An enzyme complex designated DICER COMPLEX, dices the VGAM1428 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1428 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1428 RNA is designated SEQ ID:36358, and is provided hereinbelow with reference to the sequence listing part.

[19952] VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1428 host target RNA, herein designated



VGAM HOST TARGET RNA. VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19953] VGAM1428 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1428 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1428 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19954] The complementary binding of VGAM1428 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1428 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19955] It is appreciated that VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1428 host target genes. The mRNA of each one of this plurality of VGAM1428 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1428 RNA, herein designated VGAM RNA, and which when bound by VGAM1428 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1428 host target proteins.

[19956] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1428 gene, herein designated VGAM GENE, on one or more VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19957] It is yet further appreciated that a function of VGAM1428 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1428 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2.

Specific functions, and accordingly utilities, of VGAM1428 correlate with, and may be deduced from, the identity of the host target genes which VGAM1428 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19958] Nucleotide sequences of the VGAM1428 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1428 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1428 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1428 are further described hereinbelow with reference to Table 1.

[19959] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1428 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19960] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1429 (VGAM1429) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[19961] VGAM1429 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1429 was detected is described hereinabove with reference to Figs. 2–8.

[19962] VGAM1429 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1429 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19963] VGAM1429 gene, herein designated VGAM GENE, encodes a VGAM1429 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1429 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1429 precursor RNA is designated SEQ ID:36373, and is provided hereinbelow with reference to the sequence listing part.

[19964] VGAM1429 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1429 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19965] An enzyme complex designated DICER COMPLEX, dices the VGAM1429 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1429 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1429 RNA is designated SEQ ID:36374, and is provided hereinbelow with reference to the sequence listing part.

[19966] VGAM1429 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1429 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19967] VGAM1429 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1429 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1429 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19968] The complementary binding of VGAM1429 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1429 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19969] It is appreciated that VGAM1429 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1429 host target genes. The mRNA of each one of this plurality of VGAM1429 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1429 RNA, herein designated VGAM RNA, and which when bound by VGAM1429 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1429 host target proteins.



[19970] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1429 gene, herein designated VGAM GENE, on one or more VGAM1429 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19971] It is yet further appreciated that a function of VGAM1429 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1429 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1429

correlate with, and may be deduced from, the identity of the host target genes which VGAM1429 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19972] Nucleotide sequences of the VGAM1429 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1429 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1429 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1429 are further described hereinbelow with reference to Table 1.

[19973] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1429 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19974] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1430 (VGAM1430) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[19975] VGAM1430 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1430 was detected is described hereinabove with reference to Figs. 2–8.

[19976] VGAM1430 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1430 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19977] VGAM1430 gene, herein designated VGAM GENE, encodes a VGAM1430 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1430 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1430 precursor RNA is designated SEQ ID:36447, and is provided hereinbelow with reference to the sequence listing part.

[19978] VGAM1430 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19979] An enzyme complex designated DICER COMPLEX, dices the VGAM1430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1430 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1430 RNA is designated SEQ ID:36448, and is provided hereinbelow with reference to the sequence listing part.

[19980] VGAM1430 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19981] VGAM1430 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1430 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19982] The complementary binding of VGAM1430 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1430 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19983] It is appreciated that VGAM1430 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1430 host target genes. The mRNA of each one of this plurality of VGAM1430 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1430 RNA, herein designated VGAM RNA, and which when bound by VGAM1430 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1430 host target proteins.

[19984] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1430 gene, herein designated VGAM GENE, on one or more VGAM1430 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19985] It is yet further appreciated that a function of VGAM1430 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1430 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1430 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[19986] Nucleotide sequences of the VGAM1430 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1430 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1430 are further described hereinbelow with reference to Table 1.

[19987] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1430 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[19988] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1431 (VGAM1431) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[19989] VGAM1431 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1431 was detected is described hereinabove with reference to Figs. 2-8.

[19990] VGAM1431 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Japanese iris necrotic ring virus. VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[19991] VGAM1431 gene, herein designated VGAM GENE, encodes a VGAM1431 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1431 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1431 precursor RNA is designated SEQ ID:36455, and is provided hereinbelow with reference to the sequence listing part.

[19992] VGAM1431 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[19993] An enzyme complex designated DICER COMPLEX, dices the VGAM1431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1431 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1431 RNA is designated SEQ ID:36456, and is provided hereinbelow with reference to the sequence listing part.

[19994] VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[19995] VGAM1431 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1431 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1431 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[19996] The complementary binding of VGAM1431 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1431 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[19997] It is appreciated that VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1431 host target genes. The mRNA of each one of this plurality of VGAM1431 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1431 RNA, herein designated VGAM RNA, and which when bound by VGAM1431 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1431 host target proteins.

[19998] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1431 gene, herein designated VGAM GENE, on one or more VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[19999] It is yet further appreciated that a function of VGAM1431 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1431 include diagnosis, prevention and treatment of viral infection by Japanese iris necrotic ring virus. Specific functions, and accordingly utilities, of VGAM1431 correlate with, and may be deduced from, the identity of the host target genes which VGAM1431 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20000] Nucleotide sequences of the VGAM1431 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1431 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1431 are further described hereinbelow with reference to Table 1.

[20001] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1431 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20002] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1432 (VGAM1432) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20003] VGAM1432 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1432 was detected is described hereinabove with reference to Figs. 2–8.

[20004] VGAM1432 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rubella virus.

VGAM1432 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20005] VGAM1432 gene, herein designated VGAM GENE, encodes a VGAM1432 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1432 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1432 precursor RNA is designated SEQ ID:36468, and is provided hereinbelow with reference to the sequence listing part.

[20006] VGAM1432 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20007] An enzyme complex designated DICER COMPLEX, dices the VGAM1432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1432 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1432 RNA is designated SEQ ID:36469, and is provided hereinbelow with reference to the sequence listing part.

[20008] VGAM1432 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and



a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20009] VGAM1432 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1432 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[20010] The complementary binding of VGAM1432 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1432 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20011] It is appreciated that VGAM1432 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1432 host target genes. The mRNA of each one of this plurality of VGAM1432 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1432 RNA, herein designated VGAM RNA, and which when bound by VGAM1432 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1432 host target proteins.

[20012] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1432 gene, herein designated VGAM GENE, on one or more VGAM1432 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20013] It is yet further appreciated that a function of VGAM1432 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of viral infection by Rubella virus. Specific functions, and accordingly utilities, of VGAM1432 correlate with, and may be deduced from, the identity of the host target genes which VGAM1432 binds and inhibits, and the function of these host target genes, as elaborated herein—

below.

[20014] Nucleotide sequences of the VGAM1432 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1432 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1432 are further described hereinbelow with reference to Table 1.

[20015] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1432 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20016] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1433 (VGAM1433) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20017] VGAM1433 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1433 was detected is described hereinabove with reference to Figs. 2–8.

[20018] VGAM1433 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tobacco mild green mosaic virus. VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20019] VGAM1433 gene, herein designated VGAM GENE, encodes a VGAM1433 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1433 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1433 precursor RNA is designated SEQ ID:36478, and is provided hereinbelow with reference to the sequence listing part.

[20020] VGAM1433 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20021] An enzyme complex designated DICER COMPLEX, dices the VGAM1433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1433 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1433 RNA is designated SEQ ID:36479, and is provided hereinbelow with reference to the sequence listing part.

[20022] VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[20023] VGAM1433 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1433 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20024] The complementary binding of VGAM1433 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1433 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20025] It is appreciated that VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1433 host target genes. The mRNA of each one of this plurality of VGAM1433 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1433 RNA, herein designated VGAM RNA, and which when bound by VGAM1433 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1433 host target proteins.

[20026] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1433 gene, herein designated VGAM GENE, on one



or more VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20027] It is yet further appreciated that a function of VGAM1433 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of viral infection by Tobacco mild green mosaic virus. Specific functions, and accordingly utilities, of VGAM1433 correlate with, and may be deduced from, the identity of the host target genes which VGAM1433 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20028] Nucleotide sequences of the VGAM1433 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1433 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1433 are further described hereinbelow with reference to Table 1.

[20029] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1433 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20030] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1434 (VGAM1434) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20031] VGAM1434 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1434 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[20032] VGAM1434 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 89. VGAM1434 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20033] VGAM1434 gene, herein designated VGAM GENE, encodes a VGAM1434 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1434 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1434 precursor RNA is designated SEQ ID:36486, and is provided hereinbelow with reference to the sequence listing part.

[20034] VGAM1434 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20035] An enzyme complex designated DICER COMPLEX, dices the VGAM1434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1434 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1434 RNA is designated SEQ ID:36487, and is provided hereinbelow with reference to the sequence listing part.

[20036] VGAM1434 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20037] VGAM1434 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1434 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1434 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20038] The complementary binding of VGAM1434 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1434 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20039] It is appreciated that VGAM1434 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1434 host target genes. The mRNA of each one of this plurality of VGAM1434 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1434 RNA, herein designated VGAM RNA, and which when bound by VGAM1434 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1434 host target proteins.

[20040] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1434 gene, herein designated VGAM GENE, on one or more VGAM1434 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20041] It is yet further appreciated that a function of VGAM1434 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 89. Specific functions, and accordingly utilities, of VGAM1434 correlate with, and may be deduced from, the identity of the host target genes which VGAM1434 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20042] Nucleotide sequences of the VGAM1434 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1434 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1434 are further described hereinbelow with reference to Table 1.

[20043] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1434 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20044] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1435 (VGAM1435) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20045] VGAM1435 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1435 was detected is described hereinabove with reference to Figs. 2-8.



[20046] VGAM1435 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 89. VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20047] VGAM1435 gene, herein designated VGAM GENE, encodes a VGAM1435 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1435 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1435 precursor RNA is designated SEQ ID:36501, and is provided hereinbelow with reference to the sequence listing part.

[20048] VGAM1435 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[20049] An enzyme complex designated DICER COMPLEX, dices the VGAM1435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1435 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1435 RNA is designated SEQ ID:36502, and is provided hereinbelow with reference to the sequence listing part.

[20050] VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20051] VGAM1435 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1435 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20052] The complementary binding of VGAM1435 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1435 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20053] It is appreciated that VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1435 host target genes. The mRNA of each one of this plurality of VGAM1435 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1435 RNA, herein designated VGAM RNA, and which when bound by VGAM1435 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1435 host target proteins.

[20054] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1435 gene, herein designated VGAM GENE, on one or more VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20055] It is yet further appreciated that a function of VGAM1435 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 89. Specific functions, and accordingly utilities, of VGAM1435 correlate with, and may be deduced from, the identity of the host target genes which VGAM1435 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20056] Nucleotide sequences of the VGAM1435 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1435 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1435 are further described hereinbelow with reference to Table 1.

[20057] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1435 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20058] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1436 (VGAM1436) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20059] VGAM1436 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1436 was detected is described hereinabove with reference to Figs. 2-8.

[20060] VGAM1436 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human adenovirus D. VGAM1436 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20061] VGAM1436 gene, herein designated VGAM GENE, encodes a VGAM1436 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1436 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1436 precursor RNA is designated SEQ ID:36537, and is provided hereinbelow with reference to the sequence listing part.

[20062] VGAM1436 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1436 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20063] An enzyme complex designated DICER COMPLEX, dices the VGAM1436 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1436 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1436 RNA is designated SEQ ID:36538, and is provided hereinbelow with reference to the sequence listing part.

[20064] VGAM1436 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20065] VGAM1436 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites



located in untranslated regions of VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1436 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1436 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20066] The complementary binding of VGAM1436 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1436 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1436 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20067] It is appreciated that VGAM1436 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1436 host target genes. The mRNA of each one of this plurality of VGAM1436 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1436 RNA, herein designated VGAM RNA, and which when bound by VGAM1436 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1436 host target proteins.

[20068] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1436 gene, herein designated VGAM GENE, on one or more VGAM1436 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20069] It is yet further appreciated that a function of VGAM1436 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1436 include diagnosis, prevention and treatment of viral infection by Human adenovirus D. Specific functions, and accordingly utilities, of VGAM1436 correlate with, and may be deduced from, the identity of the host target genes which VGAM1436 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20070] Nucleotide sequences of the VGAM1436 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1436 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1436 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1436 are further described hereinbelow with reference to Table 1.

[20071] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1436 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20072] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1437 (VGAM1437) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20073] VGAM1437 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1437 was detected is described hereinabove with reference to Figs. 2-8.

[20074] VGAM1437 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus

type 89. VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20075] VGAM1437 gene, herein designated VGAM GENE, encodes a VGAM1437 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1437 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1437 precursor RNA is designated SEQ ID:36556, and is provided hereinbelow with reference to the sequence listing part.

[20076] VGAM1437 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1437 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20077] An enzyme complex designated DICER COMPLEX, dices

the VGAM1437 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1437 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1437 RNA is designated SEQ ID:36557, and is provided hereinbelow with reference to the sequence listing part.

[20078] VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20079] VGAM1437 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1437 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1437 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1437 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20080] The complementary binding of VGAM1437 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1437 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20081] It is appreciated that VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1437 host target genes. The mRNA of each one of this plurality of VGAM1437 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1437 RNA, herein designated VGAM RNA, and which when bound by VGAM1437 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1437 host target proteins.

[20082] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1437 gene, herein designated VGAM GENE, on one or more VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20083] It is yet further appreciated that a function of VGAM1437 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1437 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 89. Specific functions, and accordingly utilities, of VGAM1437 correlate with, and may be deduced from, the identity of the host target genes which VGAM1437 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20084] Nucleotide sequences of the VGAM1437 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1437 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1437 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1437 are further described hereinbelow with reference to Table 1.

[20085] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1437 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20086] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1438 (VGAM1438) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20087] VGAM1438 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1438 was detected is described hereinabove with reference to Figs. 2-8.

[20088] VGAM1438 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 34. VGAM1438 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20089] VGAM1438 gene, herein designated VGAM GENE, encodes a VGAM1438 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1438 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1438 precursor RNA is designated SEQ ID:36568, and is provided hereinbelow with reference to the sequence listing part.

[20090] VGAM1438 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1438 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20091] An enzyme complex designated DICER COMPLEX, dices the VGAM1438 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1438 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1438 RNA is designated SEQ ID:36569, and is provided hereinbelow with reference to the sequence listing part.

[20092] VGAM1438 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20093] VGAM1438 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1438 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1438 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20094] The complementary binding of VGAM1438 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1438

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1438 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20095] It is appreciated that VGAM1438 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1438 host target genes. The mRNA of each one of this plurality of VGAM1438 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1438 RNA, herein designated VGAM RNA, and which when bound by VGAM1438 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1438 host target proteins.

[20096] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1438 gene, herein designated VGAM GENE, on one or more VGAM1438 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20097] It is yet further appreciated that a function of VGAM1438 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1438 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 34. Specific functions, and accordingly utilities, of VGAM1438 correlate with, and may be deduced from, the identity of the host target genes which VGAM1438 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20098] Nucleotide sequences of the VGAM1438 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1438 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1438 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1438 are further described hereinbelow with reference to Table 1.

[20099] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1438 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20100] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1439 (VGAM1439) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20101] VGAM1439 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1439 was detected is described hereinabove with reference to Figs. 2-8.

[20102] VGAM1439 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck adenovirus A. VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[20103] VGAM1439 gene, herein designated VGAM GENE, encodes a VGAM1439 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1439 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1439 precursor RNA is designated SEQ ID:36580, and is provided hereinbelow with reference to the sequence listing part.

[20104] VGAM1439 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20105] An enzyme complex designated DICER COMPLEX, dices the VGAM1439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1439 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1439 RNA is designated SEQ ID:36581, and is provided hereinbelow with reference to the sequence listing part.

[20106] VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20107] VGAM1439 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1439 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20108] The complementary binding of VGAM1439 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1439 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1439 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20109] It is appreciated that VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1439 host target genes. The mRNA of each one of this plurality of VGAM1439 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1439 RNA, herein designated VGAM RNA, and which when bound by VGAM1439 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1439 host target proteins.

[20110] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1439 gene, herein designated VGAM GENE, on one or more VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20111] It is yet further appreciated that a function of VGAM1439 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of viral infection by Duck adenovirus A. Specific functions, and accordingly utilities, of VGAM1439 correlate with, and may be deduced from, the identity of the host target genes which VGAM1439 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20112] Nucleotide sequences of the VGAM1439 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1439 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1439 are further

described hereinbelow with reference to Table 1.

[20113] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1439 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20114] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1440 (VGAM1440) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20115] VGAM1440 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1440 was detected is described hereinabove with reference to Figs. 2-8.

[20116] VGAM1440 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20117] VGAM1440 gene, herein designated VGAM GENE, encodes a VGAM1440 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1440 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1440 precursor RNA is designated SEQ ID:36592, and is provided hereinbelow with reference to the sequence listing part.

[20118] VGAM1440 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20119] An enzyme complex designated DICER COMPLEX, dices the VGAM1440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1440 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1440 RNA is designated SEQ ID:36593, and is provided hereinbelow with reference to the sequence listing part.

[20120] VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20121] VGAM1440 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1440 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1440 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20122] The complementary binding of VGAM1440 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1440 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20123] It is appreciated that VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1440 host target genes. The mRNA of each one of this plurality of VGAM1440 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1440 RNA, herein designated VGAM RNA, and which when bound by VGAM1440 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1440 host target proteins.

[20124] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1440 gene, herein designated VGAM GENE, on one or more VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20125] It is yet further appreciated that a function of VGAM1440 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM1440 correlate with, and may be deduced from, the identity of the host target genes which VGAM1440 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20126] Nucleotide sequences of the VGAM1440 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1440 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1440 are further described hereinbelow with reference to Table 1.

[20127] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1440 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20128] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1441 (VGAM1441) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20129] VGAM1441 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1441 was detected is described hereinabove with reference to Figs. 2-8.

[20130] VGAM1441 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck adenovirus A. VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20131] VGAM1441 gene, herein designated VGAM GENE, encodes

a VGAM1441 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1441 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1441 precursor RNA is designated SEQ ID:36605, and is provided hereinbelow with reference to the sequence listing part.

[20132] VGAM1441 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20133] An enzyme complex designated DICER COMPLEX, dices the VGAM1441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1441 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1441 RNA is designated SEQ ID:36606, and is provided hereinbelow with reference to the sequence listing part.

[20134] VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20135] VGAM1441 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1441 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1441 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20136] The complementary binding of VGAM1441 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1441 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[20137] It is appreciated that VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1441 host target genes. The mRNA of each one of this plurality of VGAM1441 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1441 RNA, herein designated VGAM RNA, and which when bound by VGAM1441 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1441 host target proteins.

[20138] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1441 gene, herein designated VGAM GENE, on one or more VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20139] It is yet further appreciated that a function of VGAM1441 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1441 include diagnosis, prevention and treatment of viral infection by Duck adenovirus A. Specific functions, and accordingly utilities, of VGAM1441 correlate with, and may be deduced from, the identity of the host target genes which VGAM1441 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20140] Nucleotide sequences of the VGAM1441 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1441 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1441 are further described hereinbelow with reference to Table 1.

[20141] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1441 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20142] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1442 (VGAM1442) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20143] VGAM1442 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1442 was detected is described hereinabove with reference to Figs. 2-8.

[20144] VGAM1442 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana tigrina ranavirus. VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20145] VGAM1442 gene, herein designated VGAM GENE, encodes a VGAM1442 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1442 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1442 precursor RNA is designated SEQ ID:36614, and is provided hereinbelow with reference to the sequence listing part.

[20146] VGAM1442 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20147] An enzyme complex designated DICER COMPLEX, dices the VGAM1442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1442 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1442 RNA is designated SEQ ID:36615, and is provided hereinbelow with reference to the sequence listing part.

[20148] VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20149] VGAM1442 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1442 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20150] The complementary binding of VGAM1442 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1442 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20151] It is appreciated that VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1442 host target genes. The mRNA of each one of this plurality of VGAM1442 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1442 RNA, herein designated VGAM RNA, and which when bound by VGAM1442 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1442 host target proteins.

[20152] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1442 gene, herein designated VGAM GENE, on one or more VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20153] It is yet further appreciated that a function of VGAM1442 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of viral infection by *Rana tigrina* ranavirus. Specific functions, and accordingly utilities, of VGAM1442 correlate with, and may be deduced from, the identity of the host target genes which VGAM1442 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20154] Nucleotide sequences of the VGAM1442 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1442 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1442 are further described hereinbelow with reference to Table 1.

[20155] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1442 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20156] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1443 (VGAM1443) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20157] VGAM1443 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1443 was detected is described hereinabove with reference to Figs. 2-8.

[20158] VGAM1443 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human papillomavirus type 34. VGAM1443 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20159] VGAM1443 gene, herein designated VGAM GENE, encodes a VGAM1443 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-



like most ordinary genes, VGAM1443 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1443 precursor RNA is designated SEQ ID:36624, and is provided hereinbelow with reference to the sequence listing part.

[20160] VGAM1443 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20161] An enzyme complex designated DICER COMPLEX, dices the VGAM1443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1443 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1443 RNA is designated SEQ ID:36625, and is provided hereinbelow with reference to the sequence listing part.

[20162] VGAM1443 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20163] VGAM1443 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1443 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1443 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20164] The complementary binding of VGAM1443 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1443 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20165] It is appreciated that VGAM1443 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1443 host target genes. The mRNA of each one of this plurality of VGAM1443 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1443 RNA, herein designated VGAM RNA, and which when bound by VGAM1443 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1443 host target proteins.

[20166] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1443 gene, herein designated VGAM GENE, on one or more VGAM1443 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20167] It is yet further appreciated that a function of VGAM1443 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1443 include diagnosis, prevention and treatment of viral infection by Human papillomavirus type 34. Specific functions, and accordingly utilities, of VGAM1443 correlate with, and may be deduced from, the identity of the host target genes which VGAM1443 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20168] Nucleotide sequences of the VGAM1443 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1443 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1443 are further described hereinbelow with reference to Table 1.

[20169] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1443 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20170] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1444 (VGAM1444) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20171] VGAM1444 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1444 was detected is described hereinabove with reference to Figs. 2–8.

[20172] VGAM1444 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck adenovirus A. VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20173] VGAM1444 gene, herein designated VGAM GENE, encodes a VGAM1444 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1444 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1444 precursor RNA is designated SEQ ID:36658, and is provided hereinbelow with reference to the sequence listing part.

[20174] VGAM1444 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20175] An enzyme complex designated DICER COMPLEX, dices the VGAM1444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1444 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1444 RNA is designated SEQ ID:36659, and is provided hereinbelow with reference to the sequence listing part.

[20176] VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20177] VGAM1444 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1444 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20178] The complementary binding of VGAM1444 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1444 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20179] It is appreciated that VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1444 host target genes. The mRNA of each one of this plurality of VGAM1444 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1444 RNA, herein designated VGAM RNA, and which when bound by VGAM1444 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1444 host target proteins.

[20180] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1444 gene, herein designated VGAM GENE, on one or more VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[20181] It is yet further appreciated that a function of VGAM1444 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of viral infection by Duck adenovirus A. Specific functions, and accordingly utilities, of VGAM1444 correlate with, and may be deduced from, the identity of the host target genes which VGAM1444 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20182] Nucleotide sequences of the VGAM1444 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1444 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1444 are further described hereinbelow with reference to Table 1.

[20183] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1444 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20184] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1445 (VGAM1445) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20185] VGAM1445 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1445 was detected is described hereinabove with reference to Figs. 2-8.

[20186] VGAM1445 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck adenovirus A. VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20187] VGAM1445 gene, herein designated VGAM GENE, encodes a VGAM1445 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1445 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1445 precursor RNA is designated SEQ ID:36668, and is provided hereinbelow with reference to the sequence listing part.

[20188] VGAM1445 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1445 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20189] An enzyme complex designated DICER COMPLEX, dices the VGAM1445 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1445 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM1445 RNA is designated SEQ ID:36669, and is provided hereinbelow with reference to the sequence listing part.

[20190] VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20191] VGAM1445 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1445 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1445 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20192] The complementary binding of VGAM1445 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1445 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20193] It is appreciated that VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1445 host target genes. The mRNA of

each one of this plurality of VGAM1445 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1445 RNA, herein designated VGAM RNA, and which when bound by VGAM1445 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1445 host target proteins.

[20194] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1445 gene, herein designated VGAM GENE, on one or more VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[20195] It is yet further appreciated that a function of VGAM1445 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1445 include diagnosis, prevention and treatment of viral infection by Duck adenovirus A. Specific functions, and accordingly utilities, of VGAM1445 correlate with, and may be deduced from, the identity of the host target genes which VGAM1445 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20196] Nucleotide sequences of the VGAM1445 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1445 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1445 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1445 are further described hereinbelow with reference to Table 1.

[20197] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1445 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[20198] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1446 (VGAM1446) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20199] VGAM1446 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1446 was detected is described hereinabove with reference to Figs. 2–8.

[20200] VGAM1446 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20201] VGAM1446 gene, herein designated VGAM GENE, encodes a VGAM1446 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1446 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1446 precursor RNA is designated SEQ ID:36680, and is provided hereinbelow with reference to the sequence listing part.

[20202] VGAM1446 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20203] An enzyme complex designated DICER COMPLEX, dices the VGAM1446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1446 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1446 RNA is designated SEQ ID:36681,

and is provided hereinbelow with reference to the sequence listing part.

[20204] VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20205] VGAM1446 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1446 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20206] The complementary binding of VGAM1446 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1446 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20207] It is appreciated that VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1446 host target genes. The mRNA of each one of this plurality of VGAM1446 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1446 RNA, herein designated VGAM RNA, and which when bound by VGAM1446 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1446 host target proteins.

[20208] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1446 gene, herein designated VGAM GENE, on one or more VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20209] It is yet further appreciated that a function of VGAM1446 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1446 correlate with, and may be deduced from, the identity of the host target genes which VGAM1446 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20210] Nucleotide sequences of the VGAM1446 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1446 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1446 are further described hereinbelow with reference to Table 1.

[20211] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1446 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20212] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1447 (VGAM1447) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20213] VGAM1447 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1447 was detected is described hereinabove with reference to Figs. 2–8.

[20214] VGAM1447 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20215] VGAM1447 gene, herein designated VGAM GENE, encodes a VGAM1447 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1447 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1447 precu-



sor RNA is designated SEQ ID:36686, and is provided hereinbelow with reference to the sequence listing part.

[20216] VGAM1447 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20217] An enzyme complex designated DICER COMPLEX, dices the VGAM1447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1447 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1447 RNA is designated SEQ ID:36687, and is provided hereinbelow with reference to the se-

quence listing part.

[20218] VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20219] VGAM1447 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1447 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20220] The complementary binding of VGAM1447 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1447 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20221] It is appreciated that VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1447 host target genes. The mRNA of each one of this plurality of VGAM1447 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1447 RNA, herein designated VGAM RNA, and which when bound by VGAM1447 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1447 host target proteins.

[20222] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1447 gene, herein designated VGAM GENE, on one or more VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20223] It is yet further appreciated that a function of VGAM1447

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1447 correlate with, and may be deduced from, the identity of the host target genes which VGAM1447 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20224] Nucleotide sequences of the VGAM1447 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1447 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1447 are further described hereinbelow with reference to Table 1.

[20225] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1447 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20226] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1448 (VGAM1448) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20227] VGAM1448 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1448 was detected is described hereinabove with reference to Figs. 2–8.

[20228] VGAM1448 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid herpesvirus 4. VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20229] VGAM1448 gene, herein designated VGAM GENE, encodes a VGAM1448 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1448 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1448 precursor RNA is designated SEQ ID:36691, and is provided

hereinbelow with reference to the sequence listing part.

[20230] VGAM1448 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20231] An enzyme complex designated DICER COMPLEX, dices the VGAM1448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1448 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1448 RNA is designated SEQ ID:36692, and is provided hereinbelow with reference to the sequence listing part.

[20232] VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20233] VGAM1448 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1448 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1448 RNA, herein designated



VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20234] The complementary binding of VGAM1448 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1448 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20235] It is appreciated that VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1448 host target genes. The mRNA of each one of this plurality of VGAM1448 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1448 RNA, herein designated VGAM RNA, and which when bound by VGAM1448 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1448 host target proteins.

[20236] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1448 gene, herein designated VGAM GENE, on one or more VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20237] It is yet further appreciated that a function of VGAM1448 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of viral infection by Murid herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1448 correlate with, and may be deduced from, the identity of the host target genes which VGAM1448 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20238] Nucleotide sequences of the VGAM1448 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1448 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1448 are further described hereinbelow with reference to Table 1.

[20239] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1448 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20240] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1449 (VGAM1449) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20241] VGAM1449 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1449 was detected is described hereinabove with reference to Figs. 2–8.

[20242] VGAM1449 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia virus. VGAM1449 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20243] VGAM1449 gene, herein designated VGAM GENE, encodes a VGAM1449 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1449 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1449 precursor RNA is designated SEQ ID:36708, and is provided hereinbelow with reference to the sequence listing part.

[20244] VGAM1449 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20245] An enzyme complex designated DICER COMPLEX, dices the VGAM1449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1449 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1449 RNA is designated SEQ ID:36709, and is provided hereinbelow with reference to the sequence listing part.

[20246] VGAM1449 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20247] VGAM1449 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1449 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20248] The complementary binding of VGAM1449 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1449 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20249] It is appreciated that VGAM1449 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1449 host target genes. The mRNA of each one of this plurality of VGAM1449 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1449 RNA, herein designated VGAM

RNA, and which when bound by VGAM1449 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1449 host target proteins.

[20250] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1449 gene, herein designated VGAM GENE, on one or more VGAM1449 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20251] It is yet further appreciated that a function of VGAM1449 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM1449 include diagnosis, prevention and treatment of viral infection by Ectromelia virus. Specific functions, and accordingly utilities, of VGAM1449 correlate with, and may be deduced from, the identity of the host target genes which VGAM1449 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20252] Nucleotide sequences of the VGAM1449 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1449 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1449 are further described hereinbelow with reference to Table 1.

[20253] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1449 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20254] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1450 (VGAM1450) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20255] VGAM1450 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1450 was detected is described hereinabove with reference to Figs. 2–8.

[20256] VGAM1450 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox virus. VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20257] VGAM1450 gene, herein designated VGAM GENE, encodes a VGAM1450 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1450 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1450 precursor RNA is designated SEQ ID:36722, and is provided hereinbelow with reference to the sequence listing part.

[20258] VGAM1450 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20259] An enzyme complex designated DICER COMPLEX, dices the VGAM1450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1450 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1450 RNA is designated SEQ ID:36723, and is provided hereinbelow with reference to the sequence listing part.

[20260] VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20261] VGAM1450 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1450 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1450 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1450 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20262] The complementary binding of VGAM1450 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1450 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20263] It is appreciated that VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1450 host target genes. The mRNA of each one of this plurality of VGAM1450 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1450 RNA, herein designated VGAM RNA, and which when bound by VGAM1450 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1450 host target proteins.

[20264] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1450 gene, herein designated VGAM GENE, on one or more VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20265] It is yet further appreciated that a function of VGAM1450 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1450 include diagnosis, prevention and

treatment of viral infection by Camelpox virus. Specific functions, and accordingly utilities, of VGAM1450 correlate with, and may be deduced from, the identity of the host target genes which VGAM1450 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20266] Nucleotide sequences of the VGAM1450 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1450 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1450 are further described hereinbelow with reference to Table 1.

[20267] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1450 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20268] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1451 (VGAM1451) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20269] VGAM1451 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1451 was detected is described hereinabove with reference to Figs. 2–8.

[20270] VGAM1451 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic tymovirus. VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20271] VGAM1451 gene, herein designated VGAM GENE, encodes a VGAM1451 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1451 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1451 precursor RNA is designated SEQ ID:36729, and is provided hereinbelow with reference to the sequence listing part.

[20272] VGAM1451 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1451 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20273] An enzyme complex designated DICER COMPLEX, dices the VGAM1451 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1451 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1451 RNA is designated SEQ ID:36730, and is provided hereinbelow with reference to the sequence listing part.

[20274] VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1451 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20275] VGAM1451 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1451 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1451 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20276] The complementary binding of VGAM1451 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1451 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20277] It is appreciated that VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1451 host target genes. The mRNA of each one of this plurality of VGAM1451 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1451 RNA, herein designated VGAM RNA, and which when bound by VGAM1451 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1451 host target proteins.

[20278] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1451 gene, herein designated VGAM GENE, on one or more VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20279] It is yet further appreciated that a function of VGAM1451 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1451 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus.

Specific functions, and accordingly utilities, of VGAM1451 correlate with, and may be deduced from, the identity of the host target genes which VGAM1451 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20280] Nucleotide sequences of the VGAM1451 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1451 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1451 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1451 are further described hereinbelow with reference to Table 1.

[20281] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1451 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20282] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1452 (VGAM1452) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[20283] VGAM1452 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1452 was detected is described hereinabove with reference to Figs. 2–8.

[20284] VGAM1452 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic tymovirus. VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20285] VGAM1452 gene, herein designated VGAM GENE, encodes a VGAM1452 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1452 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1452 precursor RNA is designated SEQ ID:36743, and is provided hereinbelow with reference to the sequence listing part.

[20286] VGAM1452 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1452 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20287] An enzyme complex designated DICER COMPLEX, dices the VGAM1452 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1452 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1452 RNA is designated SEQ ID:36744, and is provided hereinbelow with reference to the sequence listing part.

[20288] VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1452 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20289] VGAM1452 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1452 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20290] The complementary binding of VGAM1452 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1452 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20291] It is appreciated that VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1452 host target genes. The mRNA of each one of this plurality of VGAM1452 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1452 RNA, herein designated VGAM RNA, and which when bound by VGAM1452 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1452 host target proteins.

[20292] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1452 gene, herein designated VGAM GENE, on one or more VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20293] It is yet further appreciated that a function of VGAM1452 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus. Specific functions, and accordingly utilities, of VGAM1452

correlate with, and may be deduced from, the identity of the host target genes which VGAM1452 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20294] Nucleotide sequences of the VGAM1452 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1452 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1452 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1452 are further described hereinbelow with reference to Table 1.

[20295] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1452 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20296] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1453 (VGAM1453) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[20297] VGAM1453 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1453 was detected is described hereinabove with reference to Figs. 2–8.

[20298] VGAM1453 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV–1. VGAM1453 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20299] VGAM1453 gene, herein designated VGAM GENE, encodes a VGAM1453 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1453 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1453 precursor RNA is designated SEQ ID:36748, and is provided hereinbelow with reference to the sequence listing part.

[20300] VGAM1453 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20301] An enzyme complex designated DICER COMPLEX, dices the VGAM1453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1453 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1453 RNA is designated SEQ ID:36749, and is provided hereinbelow with reference to the sequence listing part.

[20302] VGAM1453 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20303] VGAM1453 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1453 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20304] The complementary binding of VGAM1453 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1453 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20305] It is appreciated that VGAM1453 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1453 host target genes. The mRNA of each one of this plurality of VGAM1453 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1453 RNA, herein designated VGAM RNA, and which when bound by VGAM1453 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1453 host target proteins.

[20306] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1453 gene, herein designated VGAM GENE, on one or more VGAM1453 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20307] It is yet further appreciated that a function of VGAM1453 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-1. Specific functions, and accordingly utilities, of VGAM1453 correlate with, and may be deduced from, the identity of



the host target genes which VGAM1453 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20308] Nucleotide sequences of the VGAM1453 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1453 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1453 are further described hereinbelow with reference to Table 1.

[20309] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1453 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20310] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1454 (VGAM1454) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20311] VGAM1454 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1454 was detected is described hereinabove with reference to Figs. 2–8.

[20312] VGAM1454 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic tymovirus. VGAM1454 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20313] VGAM1454 gene, herein designated VGAM GENE, encodes a VGAM1454 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1454 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1454 precursor RNA is designated SEQ ID:36792, and is provided hereinbelow with reference to the sequence listing part.

[20314] VGAM1454 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1454 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20315] An enzyme complex designated DICER COMPLEX, dices the VGAM1454 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1454 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1454 RNA is designated SEQ ID:36793, and is provided hereinbelow with reference to the sequence listing part.

[20316] VGAM1454 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20317] VGAM1454 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1454 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20318] The complementary binding of VGAM1454 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1454 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20319] It is appreciated that VGAM1454 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1454 host target genes. The mRNA of each one of this plurality of VGAM1454 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1454 RNA, herein designated VGAM RNA, and which when bound by VGAM1454 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1454 host target proteins.

[20320] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1454 gene, herein designated VGAM GENE, on one or more VGAM1454 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20321] It is yet further appreciated that a function of VGAM1454 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus. Specific functions, and accordingly utilities, of VGAM1454 correlate with, and may be deduced from, the identity of the host target genes which VGAM1454 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[20322] Nucleotide sequences of the VGAM1454 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1454 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1454 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1454 are further described hereinbelow with reference to Table 1.

[20323] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1454 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20324] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1455 (VGAM1455) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20325] VGAM1455 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1455 was detected is described hereinabove with reference to Figs. 2–8.

[20326] VGAM1455 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV–1. VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20327] VGAM1455 gene, herein designated VGAM GENE, encodes a VGAM1455 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1455 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1455 precursor RNA is designated SEQ ID:36803, and is provided hereinbelow with reference to the sequence listing part.

[20328] VGAM1455 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the



fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20329] An enzyme complex designated DICER COMPLEX, dices the VGAM1455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1455 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1455 RNA is designated SEQ ID:36804, and is provided hereinbelow with reference to the sequence listing part.

[20330] VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20331] VGAM1455 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1455 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1455 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[20332] The complementary binding of VGAM1455 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1455 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20333] It is appreciated that VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1455 host target genes. The mRNA of each one of this plurality of VGAM1455 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1455 RNA, herein designated VGAM RNA, and which when bound by VGAM1455 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1455 host target proteins.

[20334] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1455 gene, herein designated VGAM GENE, on one or more VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20335] It is yet further appreciated that a function of VGAM1455 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1455 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-1. Specific functions, and accordingly utilities, of VGAM1455 correlate with, and may be deduced from, the identity of the host target genes which VGAM1455 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[20336] Nucleotide sequences of the VGAM1455 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1455 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1455 are further described hereinbelow with reference to Table 1.

[20337] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1455 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20338] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1456 (VGAM1456) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20339] VGAM1456 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1456 was detected is described hereinabove with reference to Figs. 2–8.

[20340] VGAM1456 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus virus SIRV–1. VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20341] VGAM1456 gene, herein designated VGAM GENE, encodes a VGAM1456 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1456 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1456 precursor RNA is designated SEQ ID:36819, and is provided hereinbelow with reference to the sequence listing part.

[20342] VGAM1456 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1456 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20343] An enzyme complex designated DICER COMPLEX, dices the VGAM1456 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1456 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1456 RNA is designated SEQ ID:36820, and is provided hereinbelow with reference to the sequence listing part.

[20344] VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[20345] VGAM1456 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1456 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[20346] The complementary binding of VGAM1456 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1456 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20347] It is appreciated that VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1456 host target genes. The mRNA of each one of this plurality of VGAM1456 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1456 RNA, herein designated VGAM RNA, and which when bound by VGAM1456 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1456 host target proteins.

[20348] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1456 gene, herein designated VGAM GENE, on one

or more VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20349] It is yet further appreciated that a function of VGAM1456 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of viral infection by Sulfolobus virus SIRV-1. Specific functions, and accordingly utilities, of VGAM1456 correlate with, and may be deduced from, the identity of the host target genes which VGAM1456 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20350] Nucleotide sequences of the VGAM1456 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1456 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1456 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1456 are further described hereinbelow with reference to Table 1.

[20351] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1456 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20352] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1457 (VGAM1457) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20353] VGAM1457 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1457 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[20354] VGAM1457 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic tymovirus. VGAM1457 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20355] VGAM1457 gene, herein designated VGAM GENE, encodes a VGAM1457 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1457 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1457 precursor RNA is designated SEQ ID:36842, and is provided hereinbelow with reference to the sequence listing part.

[20356] VGAM1457 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1457 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20357] An enzyme complex designated DICER COMPLEX, dices the VGAM1457 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1457 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1457 RNA is designated SEQ ID:36843, and is provided hereinbelow with reference to the sequence listing part.

[20358] VGAM1457 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20359] VGAM1457 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1457 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1457 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20360] The complementary binding of VGAM1457 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1457 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20361] It is appreciated that VGAM1457 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1457 host target genes. The mRNA of each one of this plurality of VGAM1457 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1457 RNA, herein designated VGAM RNA, and which when bound by VGAM1457 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1457 host target proteins.

[20362] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1457 gene, herein designated VGAM GENE, on one or more VGAM1457 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20363] It is yet further appreciated that a function of VGAM1457 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1457 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus. Specific functions, and accordingly utilities, of VGAM1457 correlate with, and may be deduced from, the identity of the host target genes which VGAM1457 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20364] Nucleotide sequences of the VGAM1457 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM1457 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1457 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1457 are further described hereinbelow with reference to Table 1.

[20365] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1457 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20366] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1458 (VGAM1458) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20367] VGAM1458 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1458 was detected is described hereinabove with reference to Figs. 2-8.

[20368] VGAM1458 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic tymovirus. VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20369] VGAM1458 gene, herein designated VGAM GENE, encodes a VGAM1458 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1458 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1458 precursor RNA is designated SEQ ID:36880, and is provided hereinbelow with reference to the sequence listing part.

[20370] VGAM1458 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1458 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[20371] An enzyme complex designated DICER COMPLEX, dices the VGAM1458 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1458 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1458 RNA is designated SEQ ID:36881, and is provided hereinbelow with reference to the sequence listing part.

[20372] VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20373] VGAM1458 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1458 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20374] The complementary binding of VGAM1458 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1458 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20375] It is appreciated that VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1458 host target genes. The mRNA of each one of this plurality of VGAM1458 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1458 RNA, herein designated VGAM RNA, and which when bound by VGAM1458 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1458 host target proteins.

[20376] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1458 gene, herein designated VGAM GENE, on one or more VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20377] It is yet further appreciated that a function of VGAM1458 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus. Specific functions, and accordingly utilities, of VGAM1458 correlate with, and may be deduced from, the identity of the host target genes which VGAM1458 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20378] Nucleotide sequences of the VGAM1458 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1458 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1458 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1458 are further described hereinbelow with reference to Table 1.

[20379] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1458 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20380] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1459 (VGAM1459) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20381] VGAM1459 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1459 was detected is described hereinabove with reference to Figs. 2-8.

[20382] VGAM1459 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Tick-borne encephalitis virus. VGAM1459 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20383] VGAM1459 gene, herein designated VGAM GENE, encodes a VGAM1459 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1459 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1459 precursor RNA is designated SEQ ID:36900, and is provided hereinbelow with reference to the sequence listing part.

[20384] VGAM1459 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1459 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[20385] An enzyme complex designated DICER COMPLEX, dices the VGAM1459 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1459 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1459 RNA is designated SEQ ID:36901, and is provided hereinbelow with reference to the sequence listing part.

[20386] VGAM1459 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20387] VGAM1459 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1459 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20388] The complementary binding of VGAM1459 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1459 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1459 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20389] It is appreciated that VGAM1459 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1459 host target genes. The mRNA of each one of this plurality of VGAM1459 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1459 RNA, herein designated VGAM RNA, and which when bound by VGAM1459 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1459 host target proteins.

[20390] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1459 gene, herein designated VGAM GENE, on one or more VGAM1459 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20391] It is yet further appreciated that a function of VGAM1459 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of viral infection by Tick-borne encephalitis virus. Specific functions, and accordingly utilities, of VGAM1459 correlate with, and may be deduced from, the identity of the host target genes which VGAM1459 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20392] Nucleotide sequences of the VGAM1459 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1459 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1459 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1459 are further described hereinbelow with reference to Table 1.

[20393] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1459 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20394] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1460 (VGAM1460) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20395] VGAM1460 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1460 was detected is described hereinabove with reference to Figs. 2-8.

[20396] VGAM1460 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic ty-

movirus. VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20397] VGAM1460 gene, herein designated VGAM GENE, encodes a VGAM1460 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1460 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1460 precursor RNA is designated SEQ ID:36932, and is provided hereinbelow with reference to the sequence listing part.

[20398] VGAM1460 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20399] An enzyme complex designated DICER COMPLEX, dices the VGAM1460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1460 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1460 RNA is designated SEQ ID:36933, and is provided hereinbelow with reference to the sequence listing part.

[20400] VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20401] VGAM1460 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1460 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1460 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20402] The complementary binding of VGAM1460 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1460 host target RNA, herein designated VGAM



HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1460 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20403] It is appreciated that VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1460 host target genes. The mRNA of each one of this plurality of VGAM1460 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1460 RNA, herein designated VGAM RNA, and which when bound by VGAM1460 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1460 host target proteins.

[20404] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1460 gene, herein designated VGAM GENE, on one or more VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20405] It is yet further appreciated that a function of VGAM1460 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1460 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus. Specific functions, and accordingly utilities, of VGAM1460 correlate with, and may be deduced from, the identity of the host target genes which VGAM1460 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20406] Nucleotide sequences of the VGAM1460 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1460 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1460 are further described hereinbelow with reference to Table 1.

[20407] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1460 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20408] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1461 (VGAM1461) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20409] VGAM1461 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1461 was detected is described hereinabove with reference to Figs. 2-8.

[20410] VGAM1461 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Sphaeropsis sapinea*

RNA virus 2. VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20411] VGAM1461 gene, herein designated VGAM GENE, encodes a VGAM1461 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1461 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1461 precursor RNA is designated SEQ ID:36954, and is provided hereinbelow with reference to the sequence listing part.

[20412] VGAM1461 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20413] An enzyme complex designated DICER COMPLEX, dices

the VGAM1461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1461 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1461 RNA is designated SEQ ID:36955, and is provided hereinbelow with reference to the sequence listing part.

[20414] VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20415] VGAM1461 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1461 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1461 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1461 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20416] The complementary binding of VGAM1461 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1461 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20417] It is appreciated that VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1461 host target genes. The mRNA of each one of this plurality of VGAM1461 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1461 RNA, herein designated VGAM RNA, and which when bound by VGAM1461 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1461 host target proteins.

[20418] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1461 gene, herein designated VGAM GENE, on one or more VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20419] It is yet further appreciated that a function of VGAM1461 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1461 include diagnosis, prevention and treatment of viral infection by Sphaeropsis sapinea RNA virus 2. Specific functions, and accordingly utilities, of VGAM1461 correlate with, and may be deduced from, the identity of the host target genes which VGAM1461 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20420] Nucleotide sequences of the VGAM1461 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1461 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of



VGAM1461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1461 are further described hereinbelow with reference to Table 1.

[20421] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1461 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20422] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1462 (VGAM1462) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20423] VGAM1462 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1462 was detected is described hereinabove with reference to Figs. 2-8.

[20424] VGAM1462 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic tymovirus. VGAM1462 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20425] VGAM1462 gene, herein designated VGAM GENE, encodes a VGAM1462 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1462 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1462 precursor RNA is designated SEQ ID:36968, and is provided hereinbelow with reference to the sequence listing part.

[20426] VGAM1462 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1462 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20427] An enzyme complex designated DICER COMPLEX, dices the VGAM1462 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1462 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1462 RNA is designated SEQ ID:36969, and is provided hereinbelow with reference to the sequence listing part.

[20428] VGAM1462 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20429] VGAM1462 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1462 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20430] The complementary binding of VGAM1462 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1462

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1462 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20431] It is appreciated that VGAM1462 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1462 host target genes. The mRNA of each one of this plurality of VGAM1462 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1462 RNA, herein designated VGAM RNA, and which when bound by VGAM1462 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1462 host target proteins.

[20432] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1462 gene, herein designated VGAM GENE, on one or more VGAM1462 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20433] It is yet further appreciated that a function of VGAM1462 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus. Specific functions, and accordingly utilities, of VGAM1462 correlate with, and may be deduced from, the identity of the host target genes which VGAM1462 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20434] Nucleotide sequences of the VGAM1462 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1462 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1462 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1462 are further described hereinbelow with reference to Table 1.

[20435] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1462 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20436] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1463 (VGAM1463) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20437] VGAM1463 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1463 was detected is described hereinabove with reference to Figs. 2-8.

[20438] VGAM1463 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sphaeropsis sapinea RNA virus 2. VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[20439] VGAM1463 gene, herein designated VGAM GENE, encodes a VGAM1463 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1463 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1463 precursor RNA is designated SEQ ID:36976, and is provided hereinbelow with reference to the sequence listing part.

[20440] VGAM1463 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20441] An enzyme complex designated DICER COMPLEX, dices the VGAM1463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1463 RNA,



herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1463 RNA is designated SEQ ID:36977, and is provided hereinbelow with reference to the sequence listing part.

[20442] VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20443] VGAM1463 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1463 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1463 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20444] The complementary binding of VGAM1463 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1463 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1463 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20445] It is appreciated that VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1463 host target genes. The mRNA of each one of this plurality of VGAM1463 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1463 RNA, herein designated VGAM RNA, and which when bound by VGAM1463 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1463 host target proteins.

[20446] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1463 gene, herein designated VGAM GENE, on one or more VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20447] It is yet further appreciated that a function of VGAM1463 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1463 include diagnosis, prevention and treatment of viral infection by Sphaeropsis sapinea RNA virus 2. Specific functions, and accordingly utilities, of VGAM1463 correlate with, and may be deduced from, the identity of the host target genes which VGAM1463 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20448] Nucleotide sequences of the VGAM1463 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1463 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1463 are further

described hereinbelow with reference to Table 1.

[20449] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1463 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20450] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1464 (VGAM1464) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20451] VGAM1464 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1464 was detected is described hereinabove with reference to Figs. 2-8.

[20452] VGAM1464 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote mosaic tymovirus. VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20453] VGAM1464 gene, herein designated VGAM GENE, encodes a VGAM1464 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1464 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1464 precursor RNA is designated SEQ ID:36980, and is provided hereinbelow with reference to the sequence listing part.

[20454] VGAM1464 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20455] An enzyme complex designated DICER COMPLEX, dices the VGAM1464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1464 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1464 RNA is designated SEQ ID:36981, and is provided hereinbelow with reference to the sequence listing part.

[20456] VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20457] VGAM1464 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1464 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1464 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20458] The complementary binding of VGAM1464 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1464 host target protein, herein desig-



nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20459] It is appreciated that VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1464 host target genes. The mRNA of each one of this plurality of VGAM1464 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1464 RNA, herein designated VGAM RNA, and which when bound by VGAM1464 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1464 host target proteins.

[20460] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1464 gene, herein designated VGAM GENE, on one or more VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20461] It is yet further appreciated that a function of VGAM1464 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of viral infection by Chayote mosaic tymovirus. Specific functions, and accordingly utilities, of VGAM1464 correlate with, and may be deduced from, the identity of the host target genes which VGAM1464 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20462] Nucleotide sequences of the VGAM1464 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1464 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1464 are further described hereinbelow with reference to Table 1.

[20463] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1464 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20464] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1465 (VGAM1465) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20465] VGAM1465 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1465 was detected is described hereinabove with reference to Figs. 2-8.

[20466] VGAM1465 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20467] VGAM1465 gene, herein designated VGAM GENE, encodes

a VGAM1465 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1465 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1465 precursor RNA is designated SEQ ID:36993, and is provided hereinbelow with reference to the sequence listing part.

[20468] VGAM1465 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20469] An enzyme complex designated DICER COMPLEX, dices the VGAM1465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1465 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1465 RNA is designated SEQ ID:36994, and is provided hereinbelow with reference to the sequence listing part.

[20470] VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20471] VGAM1465 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1465 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20472] The complementary binding of VGAM1465 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1465 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[20473] It is appreciated that VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1465 host target genes. The mRNA of each one of this plurality of VGAM1465 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1465 RNA, herein designated VGAM RNA, and which when bound by VGAM1465 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1465 host target proteins.

[20474] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1465 gene, herein designated VGAM GENE, on one or more VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20475] It is yet further appreciated that a function of VGAM1465 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1465 correlate with, and may be deduced from, the identity of the host target genes which VGAM1465 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20476] Nucleotide sequences of the VGAM1465 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1465 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1465 are further described hereinbelow with reference to Table 1.

[20477] Nucleotide sequences of host target binding sites, such as



BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1465 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20478] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1466 (VGAM1466) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20479] VGAM1466 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1466 was detected is described hereinabove with reference to Figs. 2-8.

[20480] VGAM1466 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1466 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20481] VGAM1466 gene, herein designated VGAM GENE, encodes a VGAM1466 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1466 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1466 precursor RNA is designated SEQ ID:37020, and is provided hereinbelow with reference to the sequence listing part.

[20482] VGAM1466 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20483] An enzyme complex designated DICER COMPLEX, dices the VGAM1466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1466 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1466 RNA is designated SEQ ID:37021, and is provided hereinbelow with reference to the sequence listing part.

[20484] VGAM1466 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20485] VGAM1466 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1466 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20486] The complementary binding of VGAM1466 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1466 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20487] It is appreciated that VGAM1466 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1466 host target genes. The mRNA of each one of this plurality of VGAM1466 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1466 RNA, herein designated VGAM RNA, and which when bound by VGAM1466 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1466 host target proteins.

[20488] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1466 gene, herein designated VGAM GENE, on one or more VGAM1466 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20489] It is yet further appreciated that a function of VGAM1466 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1466 correlate with, and may be deduced from, the identity of the host target genes which VGAM1466 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20490] Nucleotide sequences of the VGAM1466 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1466 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1466 are further described hereinbelow with reference to Table 1.

[20491] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1466 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20492] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1467 (VGAM1467) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20493] VGAM1467 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1467 was detected is described hereinabove with reference to Figs. 2-8.

[20494] VGAM1467 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine herpesvirus 1. VGAM1467 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20495] VGAM1467 gene, herein designated VGAM GENE, encodes a VGAM1467 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1467 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1467 precursor RNA is designated SEQ ID:37037, and is provided hereinbelow with reference to the sequence listing part.

[20496] VGAM1467 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20497] An enzyme complex designated DICER COMPLEX, dices the VGAM1467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1467 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex



comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1467 RNA is designated SEQ ID:37038, and is provided hereinbelow with reference to the sequence listing part.

[20498] VGAM1467 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20499] VGAM1467 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1467 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20500] The complementary binding of VGAM1467 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1467 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20501] It is appreciated that VGAM1467 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1467 host target genes. The mRNA of each one of this plurality of VGAM1467 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1467 RNA, herein designated VGAM RNA, and which when bound by VGAM1467 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1467 host target proteins.

[20502] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1467 gene, herein designated VGAM GENE, on one or more VGAM1467 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20503] It is yet further appreciated that a function of VGAM1467 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of viral infection by Alcelaphine herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1467 correlate with, and may be deduced from, the identity of the host target genes which VGAM1467 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20504] Nucleotide sequences of the VGAM1467 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1467 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1467 are further described hereinbelow with reference to Table 1.

[20505] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1467 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20506] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1468 (VGAM1468) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20507] VGAM1468 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1468 was detected is described hereinabove with reference to Figs. 2–8.

[20508] VGAM1468 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox virus.

VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20509] VGAM1468 gene, herein designated VGAM GENE, encodes a VGAM1468 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1468 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1468 precursor RNA is designated SEQ ID:37055, and is provided hereinbelow with reference to the sequence listing part.

[20510] VGAM1468 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1468 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20511] An enzyme complex designated DICER COMPLEX, dices the VGAM1468 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1468 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1468 RNA is designated SEQ ID:37056, and is provided hereinbelow with reference to the sequence listing part.

[20512] VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20513] VGAM1468 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1468 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1468 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20514] The complementary binding of VGAM1468 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1468 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20515] It is appreciated that VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents



a plurality of VGAM1468 host target genes. The mRNA of each one of this plurality of VGAM1468 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1468 RNA, herein designated VGAM RNA, and which when bound by VGAM1468 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1468 host target proteins.

[20516] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1468 gene, herein designated VGAM GENE, on one or more VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

[20517] It is yet further appreciated that a function of VGAM1468 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1468 include diagnosis, prevention and treatment of viral infection by Cowpox virus. Specific functions, and accordingly utilities, of VGAM1468 correlate with, and may be deduced from, the identity of the host target genes which VGAM1468 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20518] Nucleotide sequences of the VGAM1468 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1468 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1468 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1468 are further described hereinbelow with reference to Table 1.

[20519] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1468 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20520] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1469 (VGAM1469) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20521] VGAM1469 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1469 was detected is described hereinabove with reference to Figs. 2-8.

[20522] VGAM1469 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian infectious bronchitis virus. VGAM1469 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20523] VGAM1469 gene, herein designated VGAM GENE, encodes a VGAM1469 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1469 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1469 precursor RNA is designated SEQ ID:37062, and is provided hereinbelow with reference to the sequence listing part.

[20524] VGAM1469 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1469 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20525] An enzyme complex designated DICER COMPLEX, dices the VGAM1469 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1469 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1469 RNA is designated SEQ ID:37063, and is provided hereinbelow with reference to the sequence listing part.

[20526] VGAM1469 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20527] VGAM1469 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1469 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20528] The complementary binding of VGAM1469 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1469 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20529] It is appreciated that VGAM1469 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1469 host target genes. The mRNA of

each one of this plurality of VGAM1469 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1469 RNA, herein designated VGAM RNA, and which when bound by VGAM1469 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1469 host target proteins.

[20530] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1469 gene, herein designated VGAM GENE, on one or more VGAM1469 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[20531] It is yet further appreciated that a function of VGAM1469 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of viral infection by Avian infectious bronchitis virus. Specific functions, and accordingly utilities, of VGAM1469 correlate with, and may be deduced from, the identity of the host target genes which VGAM1469 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20532] Nucleotide sequences of the VGAM1469 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1469 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1469 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1469 are further described hereinbelow with reference to Table 1.

[20533] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1469 RNA, herein designated VGAM RNA, are de-



scribed hereinbelow with reference to Table 2.

[20534] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1470 (VGAM1470) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20535] VGAM1470 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1470 was detected is described hereinabove with reference to Figs. 2–8.

[20536] VGAM1470 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian infectious bronchitis virus. VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20537] VGAM1470 gene, herein designated VGAM GENE, encodes a VGAM1470 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1470 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1470 precursor RNA is designated SEQ ID:37081, and is provided hereinbelow with reference to the sequence listing part.

[20538] VGAM1470 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20539] An enzyme complex designated DICER COMPLEX, dices the VGAM1470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1470 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1470 RNA is designated SEQ ID:37082,

and is provided hereinbelow with reference to the sequence listing part.

[20540] VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20541] VGAM1470 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1470 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1470 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20542] The complementary binding of VGAM1470 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1470 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20543] It is appreciated that VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1470 host target genes. The mRNA of each one of this plurality of VGAM1470 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1470 RNA, herein designated VGAM RNA, and which when bound by VGAM1470 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1470 host target proteins.

[20544] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1470 gene, herein designated VGAM GENE, on one or more VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20545] It is yet further appreciated that a function of VGAM1470 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1470 include diagnosis, prevention and treatment of viral infection by Avian infectious bronchitis virus. Specific functions, and accordingly utilities, of VGAM1470 correlate with, and may be deduced from, the identity of the host target genes which VGAM1470 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20546] Nucleotide sequences of the VGAM1470 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1470 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1470 are further described hereinbelow with reference to Table 1.

[20547] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1470 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20548] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1471 (VGAM1471) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20549] VGAM1471 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1471 was detected is described hereinabove with reference to Figs. 2–8.

[20550] VGAM1471 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian infectious bronchitis virus. VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20551] VGAM1471 gene, herein designated VGAM GENE, encodes a VGAM1471 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1471 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1471 precu-

sor RNA is designated SEQ ID:37094, and is provided hereinbelow with reference to the sequence listing part.

[20552] VGAM1471 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20553] An enzyme complex designated DICER COMPLEX, dices the VGAM1471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1471 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1471 RNA is designated SEQ ID:37095, and is provided hereinbelow with reference to the se-



quence listing part.

[20554] VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20555] VGAM1471 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1471 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20556] The complementary binding of VGAM1471 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1471 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20557] It is appreciated that VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1471 host target genes. The mRNA of each one of this plurality of VGAM1471 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1471 RNA, herein designated VGAM RNA, and which when bound by VGAM1471 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1471 host target proteins.

[20558] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1471 gene, herein designated VGAM GENE, on one or more VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20559] It is yet further appreciated that a function of VGAM1471

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1471 include diagnosis, prevention and treatment of viral infection by Avian infectious bronchitis virus. Specific functions, and accordingly utilities, of VGAM1471 correlate with, and may be deduced from, the identity of the host target genes which VGAM1471 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20560] Nucleotide sequences of the VGAM1471 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1471 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1471 are further described hereinbelow with reference to Table 1.

[20561] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1471 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20562] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1472 (VGAM1472) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20563] VGAM1472 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1472 was detected is described hereinabove with reference to Figs. 2–8.

[20564] VGAM1472 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox virus. VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20565] VGAM1472 gene, herein designated VGAM GENE, encodes a VGAM1472 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1472 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1472 precursor RNA is designated SEQ ID:37105, and is provided

hereinbelow with reference to the sequence listing part.

[20566] VGAM1472 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20567] An enzyme complex designated DICER COMPLEX, dices the VGAM1472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1472 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1472 RNA is designated SEQ ID:37106, and is provided hereinbelow with reference to the sequence listing part.

[20568] VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20569] VGAM1472 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1472 RNA, herein designated

VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20570] The complementary binding of VGAM1472 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1472 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20571] It is appreciated that VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1472 host target genes. The mRNA of each one of this plurality of VGAM1472 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-



plementary to VGAM1472 RNA, herein designated VGAM RNA, and which when bound by VGAM1472 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1472 host target proteins.

[20572] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1472 gene, herein designated VGAM GENE, on one or more VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20573] It is yet further appreciated that a function of VGAM1472 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of viral infection by Swinepox virus. Specific functions, and accordingly utilities, of VGAM1472 correlate with, and may be deduced from, the identity of the host target genes which VGAM1472 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20574] Nucleotide sequences of the VGAM1472 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1472 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1472 are further described hereinbelow with reference to Table 1.

[20575] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1472 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20576] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1473 (VGAM1473) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20577] VGAM1473 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1473 was detected is described hereinabove with reference to Figs. 2–8.

[20578] VGAM1473 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian infectious bronchitis virus. VGAM1473 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20579] VGAM1473 gene, herein designated VGAM GENE, encodes a VGAM1473 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1473 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1473 precursor RNA is designated SEQ ID:37112, and is provided hereinbelow with reference to the sequence listing part.

[20580] VGAM1473 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20581] An enzyme complex designated DICER COMPLEX, dices the VGAM1473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1473 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1473 RNA is designated SEQ ID:37113, and is provided hereinbelow with reference to the sequence listing part.

[20582] VGAM1473 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20583] VGAM1473 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1473 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20584] The complementary binding of VGAM1473 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1473 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20585] It is appreciated that VGAM1473 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1473 host target genes. The mRNA of each one of this plurality of VGAM1473 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1473 RNA, herein designated VGAM

RNA, and which when bound by VGAM1473 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1473 host target proteins.

[20586] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1473 gene, herein designated VGAM GENE, on one or more VGAM1473 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20587] It is yet further appreciated that a function of VGAM1473 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1473 include diagnosis, prevention and treatment of viral infection by Avian infectious bronchitis virus. Specific functions, and accordingly utilities, of VGAM1473 correlate with, and may be deduced from, the identity of the host target genes which VGAM1473 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20588] Nucleotide sequences of the VGAM1473 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1473 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1473 are further described hereinbelow with reference to Table 1.

[20589] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1473 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20590] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-



senger 1474 (VGAM1474) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20591] VGAM1474 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1474 was detected is described hereinabove with reference to Figs. 2-8.

[20592] VGAM1474 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian infectious bronchitis virus. VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20593] VGAM1474 gene, herein designated VGAM GENE, encodes a VGAM1474 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1474 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1474 precursor RNA is designated SEQ ID:37120, and is provided hereinbelow with reference to the sequence listing part.

[20594] VGAM1474 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20595] An enzyme complex designated DICER COMPLEX, dices the VGAM1474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1474 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1474 RNA is designated SEQ ID:37121, and is provided hereinbelow with reference to the sequence listing part.

[20596] VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20597] VGAM1474 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1474 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1474 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20598] The complementary binding of VGAM1474 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1474 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20599] It is appreciated that VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1474 host target genes. The mRNA of each one of this plurality of VGAM1474 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1474 RNA, herein designated VGAM RNA, and which when bound by VGAM1474 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1474 host target proteins.

[20600] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1474 gene, herein designated VGAM GENE, on one or more VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20601] It is yet further appreciated that a function of VGAM1474 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1474 include diagnosis, prevention and

treatment of viral infection by Avian infectious bronchitis virus. Specific functions, and accordingly utilities, of VGAM1474 correlate with, and may be deduced from, the identity of the host target genes which VGAM1474 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20602] Nucleotide sequences of the VGAM1474 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1474 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1474 are further described hereinbelow with reference to Table 1.

[20603] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1474 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20604] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1475 (VGAM1475) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20605] VGAM1475 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1475 was detected is described hereinabove with reference to Figs. 2–8.

[20606] VGAM1475 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian infectious bronchitis virus. VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20607] VGAM1475 gene, herein designated VGAM GENE, encodes a VGAM1475 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1475 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1475 precursor RNA is designated SEQ ID:37126, and is provided hereinbelow with reference to the sequence listing part.

[20608] VGAM1475 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1475 folded

precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20609] An enzyme complex designated DICER COMPLEX, dices the VGAM1475 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1475 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1475 RNA is designated SEQ ID:37127, and is provided hereinbelow with reference to the sequence listing part.

[20610] VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1475 host target RNA, herein designated



VGAM HOST TARGET RNA. VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20611] VGAM1475 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1475 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20612] The complementary binding of VGAM1475 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1475 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20613] It is appreciated that VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1475 host target genes. The mRNA of each one of this plurality of VGAM1475 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1475 RNA, herein designated VGAM RNA, and which when bound by VGAM1475 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1475 host target proteins.

[20614] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1475 gene, herein designated VGAM GENE, on one or more VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20615] It is yet further appreciated that a function of VGAM1475 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of viral infection by Avian infectious bronchitis

virus. Specific functions, and accordingly utilities, of VGAM1475 correlate with, and may be deduced from, the identity of the host target genes which VGAM1475 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20616] Nucleotide sequences of the VGAM1475 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1475 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1475 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1475 are further described hereinbelow with reference to Table 1.

[20617] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1475 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20618] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1476 (VGAM1476) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[20619] VGAM1476 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1476 was detected is described hereinabove with reference to Figs. 2–8.

[20620] VGAM1476 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian infectious bronchitis virus. VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20621] VGAM1476 gene, herein designated VGAM GENE, encodes a VGAM1476 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1476 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1476 precursor RNA is designated SEQ ID:37136, and is provided hereinbelow with reference to the sequence listing part.

[20622] VGAM1476 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1476 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20623] An enzyme complex designated DICER COMPLEX, dices the VGAM1476 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1476 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1476 RNA is designated SEQ ID:37137, and is provided hereinbelow with reference to the sequence listing part.

[20624] VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1476 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20625] VGAM1476 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1476 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-

get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20626] The complementary binding of VGAM1476 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1476 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20627] It is appreciated that VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1476 host target genes. The mRNA of each one of this plurality of VGAM1476 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1476 RNA, herein designated VGAM RNA, and which when bound by VGAM1476 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1476 host target proteins.



[20628] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1476 gene, herein designated VGAM GENE, on one or more VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20629] It is yet further appreciated that a function of VGAM1476 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of viral infection by Avian infectious bronchitis virus. Specific functions, and accordingly utilities, of

VGAM1476 correlate with, and may be deduced from, the identity of the host target genes which VGAM1476 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20630] Nucleotide sequences of the VGAM1476 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1476 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1476 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1476 are further described hereinbelow with reference to Table 1.

[20631] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1476 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20632] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1477 (VGAM1477) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[20633] VGAM1477 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1477 was detected is described hereinabove with reference to Figs. 2–8.

[20634] VGAM1477 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM1477 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20635] VGAM1477 gene, herein designated VGAM GENE, encodes a VGAM1477 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1477 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1477 precursor RNA is designated SEQ ID:37154, and is provided hereinbelow with reference to the sequence listing part.

[20636] VGAM1477 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20637] An enzyme complex designated DICER COMPLEX, dices the VGAM1477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1477 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1477 RNA is designated SEQ ID:37155, and is provided hereinbelow with reference to the sequence listing part.

[20638] VGAM1477 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20639] VGAM1477 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1477 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1477 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20640] The complementary binding of VGAM1477 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1477 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20641] It is appreciated that VGAM1477 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1477 host target genes. The mRNA of each one of this plurality of VGAM1477 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1477 RNA, herein designated VGAM RNA, and which when bound by VGAM1477 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1477 host target proteins.

[20642] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1477 gene, herein designated VGAM GENE, on one or more VGAM1477 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20643] It is yet further appreciated that a function of VGAM1477 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1477 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM1477 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1477 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20644] Nucleotide sequences of the VGAM1477 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1477 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1477 are further described hereinbelow with reference to Table 1.

[20645] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1477 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20646] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1478 (VGAM1478) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.



[20647] VGAM1478 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1478 was detected is described hereinabove with reference to Figs. 2–8.

[20648] VGAM1478 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saccharomyces cerevisiae virus L–BC (La). VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20649] VGAM1478 gene, herein designated VGAM GENE, encodes a VGAM1478 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1478 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1478 precursor RNA is designated SEQ ID:37180, and is provided hereinbelow with reference to the sequence listing part.

[20650] VGAM1478 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20651] An enzyme complex designated DICER COMPLEX, dices the VGAM1478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1478 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1478 RNA is designated SEQ ID:37181, and is provided hereinbelow with reference to the sequence listing part.

[20652] VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20653] VGAM1478 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1478 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1478 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20654] The complementary binding of VGAM1478 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1478 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20655] It is appreciated that VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1478 host target genes. The mRNA of each one of this plurality of VGAM1478 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1478 RNA, herein designated VGAM RNA, and which when bound by VGAM1478 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1478 host target proteins.

[20656] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1478 gene, herein designated VGAM GENE, on one or more VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20657] It is yet further appreciated that a function of VGAM1478 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1478 include diagnosis, prevention and treatment of viral infection by *Saccharomyces cerevisiae* virus L-BC (La). Specific functions, and accordingly utilities, of VGAM1478 correlate with, and may be deduced from, the identity of the host target genes which

VGAM1478 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20658] Nucleotide sequences of the VGAM1478 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1478 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1478 are further described hereinbelow with reference to Table 1.

[20659] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1478 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20660] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1479 (VGAM1479) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20661] VGAM1479 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1479 was detected is described hereinabove with reference to Figs. 2–8.

[20662] VGAM1479 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20663] VGAM1479 gene, herein designated VGAM GENE, encodes a VGAM1479 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1479 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1479 precursor RNA is designated SEQ ID:37187, and is provided hereinbelow with reference to the sequence listing part.

[20664] VGAM1479 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1479 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the

fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20665] An enzyme complex designated DICER COMPLEX, dices the VGAM1479 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1479 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1479 RNA is designated SEQ ID:37188, and is provided hereinbelow with reference to the sequence listing part.

[20666] VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and



a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20667] VGAM1479 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1479 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1479 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[20668] The complementary binding of VGAM1479 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1479 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20669] It is appreciated that VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1479 host target genes. The mRNA of each one of this plurality of VGAM1479 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1479 RNA, herein designated VGAM RNA, and which when bound by VGAM1479 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1479 host target proteins.

[20670] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1479 gene, herein designated VGAM GENE, on one or more VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20671] It is yet further appreciated that a function of VGAM1479 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1479 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM1479 correlate with, and may be deduced from, the identity of the host target genes which VGAM1479 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[20672] Nucleotide sequences of the VGAM1479 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1479 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1479 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1479 are further described hereinbelow with reference to Table 1.

[20673] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1479 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20674] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1480 (VGAM1480) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20675] VGAM1480 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1480 was detected is described hereinabove with reference to Figs. 2–8.

[20676] VGAM1480 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20677] VGAM1480 gene, herein designated VGAM GENE, encodes a VGAM1480 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1480 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1480 precursor RNA is designated SEQ ID:37197, and is provided hereinbelow with reference to the sequence listing part.

[20678] VGAM1480 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20679] An enzyme complex designated DICER COMPLEX, dices the VGAM1480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1480 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1480 RNA is designated SEQ ID:37198, and is provided hereinbelow with reference to the sequence listing part.

[20680] VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[20681] VGAM1480 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1480 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20682] The complementary binding of VGAM1480 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1480 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20683] It is appreciated that VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1480 host target genes. The mRNA of each one of this plurality of VGAM1480 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1480 RNA, herein designated VGAM RNA, and which when bound by VGAM1480 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1480 host target proteins.

[20684] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1480 gene, herein designated VGAM GENE, on one



or more VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20685] It is yet further appreciated that a function of VGAM1480 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM1480 correlate with, and may be deduced from, the identity of the host target genes which VGAM1480 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20686] Nucleotide sequences of the VGAM1480 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1480 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1480 are further described hereinbelow with reference to Table 1.

[20687] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1480 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20688] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1481 (VGAM1481) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20689] VGAM1481 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1481 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[20690] VGAM1481 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saccharomyces cerevisiae virus L–BC (La). VGAM1481 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20691] VGAM1481 gene, herein designated VGAM GENE, encodes a VGAM1481 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1481 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1481 precursor RNA is designated SEQ ID:37365, and is provided hereinbelow with reference to the sequence listing part.

[20692] VGAM1481 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1481 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20693] An enzyme complex designated DICER COMPLEX, dices the VGAM1481 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1481 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1481 RNA is designated SEQ ID:37366, and is provided hereinbelow with reference to the sequence listing part.

[20694] VGAM1481 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20695] VGAM1481 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1481 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20696] The complementary binding of VGAM1481 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1481 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20697] It is appreciated that VGAM1481 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1481 host target genes. The mRNA of each one of this plurality of VGAM1481 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1481 RNA, herein designated VGAM RNA, and which when bound by VGAM1481 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1481 host target proteins.

[20698] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1481 gene, herein designated VGAM GENE, on one or more VGAM1481 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20699] It is yet further appreciated that a function of VGAM1481 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of viral infection by *Saccharomyces cerevisiae* virus L-BC (La). Specific functions, and accordingly utilities, of VGAM1481 correlate with, and may be deduced from, the identity of the host target genes which VGAM1481 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20700] Nucleotide sequences of the VGAM1481 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the diced VGAM1481 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1481 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1481 are further described hereinbelow with reference to Table 1.

[20701] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1481 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20702] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1482 (VGAM1482) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20703] VGAM1482 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1482 was detected is described hereinabove with reference to Figs. 2-8.



[20704] VGAM1482 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saccharomyces cerevisiae virus L-BC (La). VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20705] VGAM1482 gene, herein designated VGAM GENE, encodes a VGAM1482 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1482 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1482 precursor RNA is designated SEQ ID:37378, and is provided hereinbelow with reference to the sequence listing part.

[20706] VGAM1482 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1482 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[20707] An enzyme complex designated DICER COMPLEX, dices the VGAM1482 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1482 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1482 RNA is designated SEQ ID:37379, and is provided hereinbelow with reference to the sequence listing part.

[20708] VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20709] VGAM1482 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1482 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1482 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20710] The complementary binding of VGAM1482 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1482 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20711] It is appreciated that VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1482 host target genes. The mRNA of each one of this plurality of VGAM1482 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1482 RNA, herein designated VGAM RNA, and which when bound by VGAM1482 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1482 host target proteins.

[20712] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1482 gene, herein designated VGAM GENE, on one or more VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20713] It is yet further appreciated that a function of VGAM1482 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1482 include diagnosis, prevention and treatment of viral infection by Saccharomyces cerevisiae virus L-BC (La). Specific functions, and accordingly utilities, of VGAM1482 correlate with, and may be deduced from, the identity of the host target genes which VGAM1482 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20714] Nucleotide sequences of the VGAM1482 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1482 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1482 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1482 are further described hereinbelow with reference to Table 1.

[20715] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1482 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20716] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1483 (VGAM1483) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20717] VGAM1483 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1483 was detected is described hereinabove with reference to Figs. 2-8.

[20718] VGAM1483 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human herpesvirus 5. VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20719] VGAM1483 gene, herein designated VGAM GENE, encodes a VGAM1483 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1483 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1483 precursor RNA is designated SEQ ID:37404, and is provided hereinbelow with reference to the sequence listing part.

[20720] VGAM1483 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20721] An enzyme complex designated DICER COMPLEX, dices the VGAM1483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1483 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1483 RNA is designated SEQ ID:37405, and is provided hereinbelow with reference to the sequence listing part.

[20722] VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20723] VGAM1483 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites



located in untranslated regions of VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1483 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20724] The complementary binding of VGAM1483 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1483 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1483 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20725] It is appreciated that VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1483 host target genes. The mRNA of each one of this plurality of VGAM1483 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1483 RNA, herein designated VGAM RNA, and which when bound by VGAM1483 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1483 host target proteins.

[20726] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1483 gene, herein designated VGAM GENE, on one or more VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20727] It is yet further appreciated that a function of VGAM1483 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1483 correlate with, and may be deduced from, the identity of the host target genes which VGAM1483 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20728] Nucleotide sequences of the VGAM1483 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1483 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1483 are further described hereinbelow with reference to Table 1.

[20729] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1483 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20730] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1484 (VGAM1484) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20731] VGAM1484 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1484 was detected is described hereinabove with reference to Figs. 2-8.

[20732] VGAM1484 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5.

VGAM1484 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20733] VGAM1484 gene, herein designated VGAM GENE, encodes a VGAM1484 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1484 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1484 precursor RNA is designated SEQ ID:37418, and is provided hereinbelow with reference to the sequence listing part.

[20734] VGAM1484 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1484 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20735] An enzyme complex designated DICER COMPLEX, dices

the VGAM1484 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1484 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1484 RNA is designated SEQ ID:37419, and is provided hereinbelow with reference to the sequence listing part.

[20736] VGAM1484 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1484 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1484 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20737] VGAM1484 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1484 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1484 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1484 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1484 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20738] The complementary binding of VGAM1484 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1484 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1484 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1484 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20739] It is appreciated that VGAM1484 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1484 host target genes. The mRNA of each one of this plurality of VGAM1484 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1484 RNA, herein designated VGAM RNA, and which when bound by VGAM1484 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1484 host target proteins.

[20740] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1484 gene, herein designated VGAM GENE, on one or more VGAM1484 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-



cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20741] It is yet further appreciated that a function of VGAM1484 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1484 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1484 correlate with, and may be deduced from, the identity of the host target genes which VGAM1484 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20742] Nucleotide sequences of the VGAM1484 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1484 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1484 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1484 are further described hereinbelow with reference to Table 1.

[20743] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1484 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20744] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1485 (VGAM1485) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20745] VGAM1485 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1485 was detected is described hereinabove with reference to Figs. 2-8.

[20746] VGAM1485 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human herpesvirus 5. VGAM1485 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[20747] VGAM1485 gene, herein designated VGAM GENE, encodes a VGAM1485 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1485 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1485 precursor RNA is designated SEQ ID:37429, and is provided hereinbelow with reference to the sequence listing part.

[20748] VGAM1485 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1485 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20749] An enzyme complex designated DICER COMPLEX, dices the VGAM1485 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1485 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1485 RNA is designated SEQ ID:37430, and is provided hereinbelow with reference to the sequence listing part.

[20750] VGAM1485 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1485 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1485 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20751] VGAM1485 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1485 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1485 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1485 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20752] The complementary binding of VGAM1485 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1485 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1485

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1485 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20753] It is appreciated that VGAM1485 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1485 host target genes. The mRNA of each one of this plurality of VGAM1485 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1485 RNA, herein designated VGAM RNA, and which when bound by VGAM1485 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1485 host target proteins.

[20754] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1485 gene, herein designated VGAM GENE, on one or more VGAM1485 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20755] It is yet further appreciated that a function of VGAM1485 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of viral infection by Human herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1485 correlate with, and may be deduced from, the identity of the host target genes which VGAM1485 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20756] Nucleotide sequences of the VGAM1485 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1485 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1485 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1485 are further described hereinbelow with reference to Table 1.

[20757] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1485 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20758] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1486 (VGAM1486) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20759] VGAM1486 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1486 was detected is described hereinabove with reference to Figs. 2-8.

[20760] VGAM1486 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human adenovirus F. VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the



human genome.

[20761] VGAM1486 gene, herein designated VGAM GENE, encodes a VGAM1486 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1486 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1486 precursor RNA is designated SEQ ID:37447, and is provided hereinbelow with reference to the sequence listing part.

[20762] VGAM1486 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1486 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20763] An enzyme complex designated DICER COMPLEX, dices the VGAM1486 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1486 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1486 RNA is designated SEQ ID:37448, and is provided hereinbelow with reference to the sequence listing part.

[20764] VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20765] VGAM1486 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1486 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1486 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20766] The complementary binding of VGAM1486 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1486 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1486 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20767] It is appreciated that VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1486 host target genes. The mRNA of each one of this plurality of VGAM1486 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1486 RNA, herein designated VGAM RNA, and which when bound by VGAM1486 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1486 host target proteins.

[20768] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1486 gene, herein designated VGAM GENE, on one or more VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20769] It is yet further appreciated that a function of VGAM1486 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1486 include diagnosis, prevention and treatment of viral infection by Human adenovirus F. Specific functions, and accordingly utilities, of VGAM1486 correlate with, and may be deduced from, the identity of the host target genes which VGAM1486 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20770] Nucleotide sequences of the VGAM1486 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1486 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1486 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1486 are further

described hereinbelow with reference to Table 1.

[20771] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1486 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20772] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1487 (VGAM1487) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20773] VGAM1487 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1487 was detected is described hereinabove with reference to Figs. 2-8.

[20774] VGAM1487 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saccharomyces cerevisiae virus L-BC (La). VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20775] VGAM1487 gene, herein designated VGAM GENE, encodes a VGAM1487 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1487 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1487 precursor RNA is designated SEQ ID:37452, and is provided hereinbelow with reference to the sequence listing part.

[20776] VGAM1487 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20777] An enzyme complex designated DICER COMPLEX, dices the VGAM1487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1487 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1487 RNA is designated SEQ ID:37453, and is provided hereinbelow with reference to the sequence listing part.

[20778] VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20779] VGAM1487 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1487 RNA, herein designated



VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1487 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20780] The complementary binding of VGAM1487 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1487 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20781] It is appreciated that VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1487 host target genes. The mRNA of each one of this plurality of VGAM1487 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1487 RNA, herein designated VGAM RNA, and which when bound by VGAM1487 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1487 host target proteins.

[20782] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1487 gene, herein designated VGAM GENE, on one or more VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20783] It is yet further appreciated that a function of VGAM1487 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of viral infection by *Saccharomyces cerevisiae* virus L-BC (La). Specific functions, and accordingly utilities, of VGAM1487 correlate with, and may be deduced from, the identity of the host target genes which VGAM1487 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20784] Nucleotide sequences of the VGAM1487 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1487 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1487 are further described hereinbelow with reference to Table 1.

[20785] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1487 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20786] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1488 (VGAM1488) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20787] VGAM1488 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1488 was detected is described hereinabove with reference to Figs. 2-8.

[20788] VGAM1488 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saccharomyces cerevisiae virus L-BC (La). VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20789] VGAM1488 gene, herein designated VGAM GENE, encodes

a VGAM1488 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1488 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1488 precursor RNA is designated SEQ ID:37462, and is provided hereinbelow with reference to the sequence listing part.

[20790] VGAM1488 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20791] An enzyme complex designated DICER COMPLEX, dices the VGAM1488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1488 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1488 RNA is designated SEQ ID:37463, and is provided hereinbelow with reference to the sequence listing part.

[20792] VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20793] VGAM1488 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1488 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20794] The complementary binding of VGAM1488 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1488 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[20795] It is appreciated that VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1488 host target genes. The mRNA of each one of this plurality of VGAM1488 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1488 RNA, herein designated VGAM RNA, and which when bound by VGAM1488 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1488 host target proteins.

[20796] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1488 gene, herein designated VGAM GENE, on one or more VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-



pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20797] It is yet further appreciated that a function of VGAM1488 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of viral infection by *Saccharomyces cerevisiae* virus L-BC (La). Specific functions, and accordingly utilities, of VGAM1488 correlate with, and may be deduced from, the identity of the host target genes which VGAM1488 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20798] Nucleotide sequences of the VGAM1488 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1488 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1488 are further described hereinbelow with reference to Table 1.

[20799] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1488 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20800] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1489 (VGAM1489) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20801] VGAM1489 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1489 was detected is described hereinabove with reference to Figs. 2-8.

[20802] VGAM1489 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1489 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20803] VGAM1489 gene, herein designated VGAM GENE, encodes a VGAM1489 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1489 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1489 precursor RNA is designated SEQ ID:37475, and is provided hereinbelow with reference to the sequence listing part.

[20804] VGAM1489 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20805] An enzyme complex designated DICER COMPLEX, dices the VGAM1489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1489 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1489 RNA is designated SEQ ID:37476, and is provided hereinbelow with reference to the sequence listing part.

[20806] VGAM1489 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20807] VGAM1489 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1489 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20808] The complementary binding of VGAM1489 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1489 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20809] It is appreciated that VGAM1489 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1489 host target genes. The mRNA of each one of this plurality of VGAM1489 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1489 RNA, herein designated VGAM RNA, and which when bound by VGAM1489 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1489 host target proteins.

[20810] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1489 gene, herein designated VGAM GENE, on one or more VGAM1489 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20811] It is yet further appreciated that a function of VGAM1489 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1489 correlate with, and may be deduced from, the identity of the host target genes which VGAM1489 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20812] Nucleotide sequences of the VGAM1489 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1489 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1489 are further described hereinbelow with reference to Table 1.

[20813] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1489 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20814] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1490 (VGAM1490) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20815] VGAM1490 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1490 was detected is described hereinabove with reference to Figs. 2-8.

[20816] VGAM1490 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1490 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20817] VGAM1490 gene, herein designated VGAM GENE, encodes a VGAM1490 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-



like most ordinary genes, VGAM1490 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1490 precursor RNA is designated SEQ ID:37485, and is provided hereinbelow with reference to the sequence listing part.

[20818] VGAM1490 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20819] An enzyme complex designated DICER COMPLEX, dices the VGAM1490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1490 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1490 RNA is designated SEQ ID:37486, and is provided hereinbelow with reference to the sequence listing part.

[20820] VGAM1490 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20821] VGAM1490 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1490 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1490 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20822] The complementary binding of VGAM1490 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1490 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20823] It is appreciated that VGAM1490 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1490 host target genes. The mRNA of each one of this plurality of VGAM1490 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1490 RNA, herein designated VGAM RNA, and which when bound by VGAM1490 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1490 host target proteins.

[20824] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1490 gene, herein designated VGAM GENE, on one or more VGAM1490 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20825] It is yet further appreciated that a function of VGAM1490 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1490 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1490 correlate with, and may be deduced from, the identity of the host target genes which VGAM1490 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20826] Nucleotide sequences of the VGAM1490 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1490 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1490 are further described hereinbelow with reference to Table 1.

[20827] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1490 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20828] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1491 (VGAM1491) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20829] VGAM1491 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1491 was detected is described hereinabove with reference to Figs. 2–8.

[20830] VGAM1491 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1491 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20831] VGAM1491 gene, herein designated VGAM GENE, encodes a VGAM1491 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1491 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1491 precursor RNA is designated SEQ ID:37498, and is provided hereinbelow with reference to the sequence listing part.

[20832] VGAM1491 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1491 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20833] An enzyme complex designated DICER COMPLEX, dices the VGAM1491 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1491 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1491 RNA is designated SEQ ID:37499, and is provided hereinbelow with reference to the sequence listing part.

[20834] VGAM1491 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20835] VGAM1491 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,



BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1491 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20836] The complementary binding of VGAM1491 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1491 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20837] It is appreciated that VGAM1491 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1491 host target genes. The mRNA of each one of this plurality of VGAM1491 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1491 RNA, herein designated VGAM RNA, and which when bound by VGAM1491 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1491 host target proteins.

[20838] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1491 gene, herein designated VGAM GENE, on one or more VGAM1491 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [20839] It is yet further appreciated that a function of VGAM1491 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1491 correlate with, and may be deduced from, the identity of the host target genes which VGAM1491 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [20840] Nucleotide sequences of the VGAM1491 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the duced VGAM1491 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1491 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1491 are further described hereinbelow with reference to Table 1.
- [20841] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1491 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20842] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1492 (VGAM1492) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20843] VGAM1492 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1492 was detected is described hereinabove with reference to Figs. 2-8.

[20844] VGAM1492 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine infectious anemia virus. VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20845] VGAM1492 gene, herein designated VGAM GENE, encodes a VGAM1492 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1492 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1492 precursor RNA is designated SEQ ID:37558, and is provided hereinbelow with reference to the sequence listing part.

[20846] VGAM1492 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20847] An enzyme complex designated DICER COMPLEX, dices the VGAM1492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1492 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide se-

quence of VGAM1492 RNA is designated SEQ ID:37559, and is provided hereinbelow with reference to the sequence listing part.

[20848] VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20849] VGAM1492 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1492 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20850] The complementary binding of VGAM1492 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1492 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20851] It is appreciated that VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1492 host target genes. The mRNA of

each one of this plurality of VGAM1492 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1492 RNA, herein designated VGAM RNA, and which when bound by VGAM1492 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1492 host target proteins.

[20852] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1492 gene, herein designated VGAM GENE, on one or more VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science



294,779 (2001)).

[20853] It is yet further appreciated that a function of VGAM1492 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of viral infection by Equine infectious anemia virus. Specific functions, and accordingly utilities, of VGAM1492 correlate with, and may be deduced from, the identity of the host target genes which VGAM1492 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20854] Nucleotide sequences of the VGAM1492 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1492 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1492 are further described hereinbelow with reference to Table 1.

[20855] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1492 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[20856] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1493 (VGAM1493) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20857] VGAM1493 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1493 was detected is described hereinabove with reference to Figs. 2–8.

[20858] VGAM1493 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine infectious anemia virus. VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20859] VGAM1493 gene, herein designated VGAM GENE, encodes a VGAM1493 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1493 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1493 precursor RNA is designated SEQ ID:37571, and is provided hereinbelow with reference to the sequence listing part.

[20860] VGAM1493 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1493 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20861] An enzyme complex designated DICER COMPLEX, dices the VGAM1493 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1493 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1493 RNA is designated SEQ ID:37572,

and is provided hereinbelow with reference to the sequence listing part.

[20862] VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20863] VGAM1493 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1493 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20864] The complementary binding of VGAM1493 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1493 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20865] It is appreciated that VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1493 host target genes. The mRNA of each one of this plurality of VGAM1493 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1493 RNA, herein designated VGAM RNA, and which when bound by VGAM1493 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1493 host target proteins.

[20866] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1493 gene, herein designated VGAM GENE, on one or more VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20867] It is yet further appreciated that a function of VGAM1493 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of viral infection by Equine infectious anemia virus. Specific functions, and accordingly utilities, of VGAM1493 correlate with, and may be deduced from, the identity of the host target genes which VGAM1493 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20868] Nucleotide sequences of the VGAM1493 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1493 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1493 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1493 are further described hereinbelow with reference to Table 1.

[20869] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1493 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20870] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1494 (VGAM1494) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20871] VGAM1494 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1494 was detected is described hereinabove with reference to Figs. 2–8.

[20872] VGAM1494 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine infectious anemia virus. VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20873] VGAM1494 gene, herein designated VGAM GENE, encodes a VGAM1494 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1494 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1494 precursor



sor RNA is designated SEQ ID:37576, and is provided hereinbelow with reference to the sequence listing part.

[20874] VGAM1494 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20875] An enzyme complex designated DICER COMPLEX, dices the VGAM1494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1494 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1494 RNA is designated SEQ ID:37577, and is provided hereinbelow with reference to the se-

quence listing part.

[20876] VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20877] VGAM1494 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not

meant to be limiting VGAM1494 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20878] The complementary binding of VGAM1494 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1494 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20879] It is appreciated that VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1494 host target genes. The mRNA of each one of this plurality of VGAM1494 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1494 RNA, herein designated VGAM RNA, and which when bound by VGAM1494 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1494 host target proteins.

[20880] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1494 gene, herein designated VGAM GENE, on one or more VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20881] It is yet further appreciated that a function of VGAM1494

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of viral infection by Equine infectious anemia virus. Specific functions, and accordingly utilities, of VGAM1494 correlate with, and may be deduced from, the identity of the host target genes which VGAM1494 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20882] Nucleotide sequences of the VGAM1494 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1494 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1494 are further described hereinbelow with reference to Table 1.

[20883] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1494 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20884] Fig. 1 further provides a conceptual description of another

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1495 (VGAM1495) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20885] VGAM1495 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1495 was detected is described hereinabove with reference to Figs. 2–8.

[20886] VGAM1495 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine infectious anemia virus. VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20887] VGAM1495 gene, herein designated VGAM GENE, encodes a VGAM1495 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1495 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1495 precursor RNA is designated SEQ ID:37587, and is provided

hereinbelow with reference to the sequence listing part.

[20888] VGAM1495 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20889] An enzyme complex designated DICER COMPLEX, dices the VGAM1495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1495 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1495 RNA is designated SEQ ID:37588, and is provided hereinbelow with reference to the sequence listing part.

[20890] VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20891] VGAM1495 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1495 RNA, herein designated



VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20892] The complementary binding of VGAM1495 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1495 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20893] It is appreciated that VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1495 host target genes. The mRNA of each one of this plurality of VGAM1495 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1495 RNA, herein designated VGAM RNA, and which when bound by VGAM1495 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1495 host target proteins.

[20894] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1495 gene, herein designated VGAM GENE, on one or more VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20895] It is yet further appreciated that a function of VGAM1495 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of viral infection by Equine infectious anemia virus. Specific functions, and accordingly utilities, of VGAM1495 correlate with, and may be deduced from, the identity of the host target genes which VGAM1495 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20896] Nucleotide sequences of the VGAM1495 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1495 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1495 are further described hereinbelow with reference to Table 1.

[20897] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1495 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20898] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present

invention, referred to here as Viral Genomic Address Messenger 1496 (VGAM1496) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20899] VGAM1496 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1496 was detected is described hereinabove with reference to Figs. 2–8.

[20900] VGAM1496 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine herpesvirus 2. VGAM1496 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20901] VGAM1496 gene, herein designated VGAM GENE, encodes a VGAM1496 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1496 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1496 precursor RNA is designated SEQ ID:37599, and is provided hereinbelow with reference to the sequence listing part.

[20902] VGAM1496 precursor RNA, herein designated VGAM PRE-CURSOR RNA, folds onto itself, forming VGAM1496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20903] An enzyme complex designated DICER COMPLEX, dices the VGAM1496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1496 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1496 RNA is designated SEQ ID:37600, and is provided hereinbelow with reference to the sequence listing part.

[20904] VGAM1496 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20905] VGAM1496 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1496 RNA, herein designated VGAM RNA, may have a different number of host target

binding sites in untranslated regions of a VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20906] The complementary binding of VGAM1496 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1496 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20907] It is appreciated that VGAM1496 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1496 host target genes. The mRNA of each one of this plurality of VGAM1496 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1496 RNA, herein designated VGAM

RNA, and which when bound by VGAM1496 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1496 host target proteins.

[20908] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1496 gene, herein designated VGAM GENE, on one or more VGAM1496 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20909] It is yet further appreciated that a function of VGAM1496 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,



utilities of VGAM1496 include diagnosis, prevention and treatment of viral infection by Saimiriine herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1496 correlate with, and may be deduced from, the identity of the host target genes which VGAM1496 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20910] Nucleotide sequences of the VGAM1496 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1496 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1496 are further described hereinbelow with reference to Table 1.

[20911] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1496 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20912] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Mes-

senger 1497 (VGAM1497) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20913] VGAM1497 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1497 was detected is described hereinabove with reference to Figs. 2-8.

[20914] VGAM1497 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Kennedya yellow mosaic virus. VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20915] VGAM1497 gene, herein designated VGAM GENE, encodes a VGAM1497 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1497 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1497 precursor RNA is designated SEQ ID:37614, and is provided hereinbelow with reference to the sequence listing part.

[20916] VGAM1497 precursor RNA, herein designated VGAM PRE-

CURSOR RNA, folds onto itself, forming VGAM1497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20917] An enzyme complex designated DICER COMPLEX, dices the VGAM1497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1497 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1497 RNA is designated SEQ ID:37615, and is provided hereinbelow with reference to the sequence listing part.

[20918] VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20919] VGAM1497 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1497 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1497 host

target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20920] The complementary binding of VGAM1497 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1497 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20921] It is appreciated that VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1497 host target genes. The mRNA of each one of this plurality of VGAM1497 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1497 RNA, herein designated VGAM RNA, and which when bound by VGAM1497 RNA, herein

designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1497 host target proteins.

[20922] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1497 gene, herein designated VGAM GENE, on one or more VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20923] It is yet further appreciated that a function of VGAM1497 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1497 include diagnosis, prevention and

treatment of viral infection by Kennedyya yellow mosaic virus. Specific functions, and accordingly utilities, of VGAM1497 correlate with, and may be deduced from, the identity of the host target genes which VGAM1497 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20924] Nucleotide sequences of the VGAM1497 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1497 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1497 are further described hereinbelow with reference to Table 1.

[20925] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1497 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20926] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1498 (VGAM1498) viral gene, which modulates ex-

pression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20927] VGAM1498 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1498 was detected is described hereinabove with reference to Figs. 2–8.

[20928] VGAM1498 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20929] VGAM1498 gene, herein designated VGAM GENE, encodes a VGAM1498 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1498 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1498 precursor RNA is designated SEQ ID:37626, and is provided hereinbelow with reference to the sequence listing part.

[20930] VGAM1498 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1498 folded



precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20931] An enzyme complex designated DICER COMPLEX, dices the VGAM1498 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1498 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1498 RNA is designated SEQ ID:37627, and is provided hereinbelow with reference to the sequence listing part.

[20932] VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1498 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20933] VGAM1498 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1498 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA.

It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20934] The complementary binding of VGAM1498 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1498 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20935] It is appreciated that VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1498 host target genes. The mRNA of each one of this plurality of VGAM1498 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1498 RNA, herein designated VGAM RNA, and which when bound by VGAM1498 RNA, herein designated VGAM RNA, causes inhibition of translation of

respective one or more VGAM1498 host target proteins.

[20936] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1498 gene, herein designated VGAM GENE, on one or more VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20937] It is yet further appreciated that a function of VGAM1498 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Spe-

cific functions, and accordingly utilities, of VGAM1498 correlate with, and may be deduced from, the identity of the host target genes which VGAM1498 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20938] Nucleotide sequences of the VGAM1498 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1498 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1498 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1498 are further described hereinbelow with reference to Table 1.

[20939] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1498 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20940] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1499 (VGAM1499) viral gene, which modulates expression of respective host target genes thereof, the func-

tion and utility of which host target genes is known in the art.

[20941] VGAM1499 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1499 was detected is described hereinabove with reference to Figs. 2–8.

[20942] VGAM1499 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Kennedya yellow mosaic virus. VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20943] VGAM1499 gene, herein designated VGAM GENE, encodes a VGAM1499 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1499 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1499 precursor RNA is designated SEQ ID:37647, and is provided hereinbelow with reference to the sequence listing part.

[20944] VGAM1499 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1499 folded precursor RNA, herein designated VGAM FOLDED PRECUR-

SOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20945] An enzyme complex designated DICER COMPLEX, dices the VGAM1499 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1499 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1499 RNA is designated SEQ ID:37648, and is provided hereinbelow with reference to the sequence listing part.

[20946] VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1499 host target RNA,

herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20947] VGAM1499 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1499 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host tar-



get binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20948] The complementary binding of VGAM1499 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1499 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20949] It is appreciated that VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1499 host target genes. The mRNA of each one of this plurality of VGAM1499 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1499 RNA, herein designated VGAM RNA, and which when bound by VGAM1499 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1499 host target proteins.

[20950] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1499 gene, herein designated VGAM GENE, on one or more VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20951] It is yet further appreciated that a function of VGAM1499 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of viral infection by Kennedy yellow mosaic virus. Specific functions, and accordingly utilities, of

VGAM1499 correlate with, and may be deduced from, the identity of the host target genes which VGAM1499 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20952] Nucleotide sequences of the VGAM1499 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1499 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1499 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1499 are further described hereinbelow with reference to Table 1.

[20953] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1499 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20954] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1500 (VGAM1500) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the

art.

[20955] VGAM1500 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1500 was detected is described hereinabove with reference to Figs. 2–8.

[20956] VGAM1500 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20957] VGAM1500 gene, herein designated VGAM GENE, encodes a VGAM1500 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1500 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1500 precursor RNA is designated SEQ ID:37658, and is provided hereinbelow with reference to the sequence listing part.

[20958] VGAM1500 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1500 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure.

As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20959] An enzyme complex designated DICER COMPLEX, dices the VGAM1500 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1500 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1500 RNA is designated SEQ ID:37659, and is provided hereinbelow with reference to the sequence listing part.

[20960] VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA, comprises

three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20961] VGAM1500 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1500 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an

example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20962] The complementary binding of VGAM1500 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1500 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20963] It is appreciated that VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1500 host target genes. The mRNA of each one of this plurality of VGAM1500 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1500 RNA, herein designated VGAM RNA, and which when bound by VGAM1500 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1500 host target proteins.

[20964] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1500 gene, herein designated VGAM GENE, on one or more VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20965] It is yet further appreciated that a function of VGAM1500 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1500 correlate with, and may be deduced from, the identity of



the host target genes which VGAM1500 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[20966] Nucleotide sequences of the VGAM1500 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1500 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1500 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1500 are further described hereinbelow with reference to Table 1.

[20967] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1500 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20968] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1501 (VGAM1501) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20969] VGAM1501 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1501 was detected is described hereinabove with reference to Figs. 2–8.

[20970] VGAM1501 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rat cytomegalovirus. VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20971] VGAM1501 gene, herein designated VGAM GENE, encodes a VGAM1501 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1501 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1501 precursor RNA is designated SEQ ID:37720, and is provided hereinbelow with reference to the sequence listing part.

[20972] VGAM1501 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typi-

cal of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20973] An enzyme complex designated DICER COMPLEX, dices the VGAM1501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1501 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1501 RNA is designated SEQ ID:37721, and is provided hereinbelow with reference to the sequence listing part.

[20974] VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding

gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20975] VGAM1501 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1501 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1501 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be lo-

cated in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[20976] The complementary binding of VGAM1501 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1501 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20977] It is appreciated that VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1501 host target genes. The mRNA of each one of this plurality of VGAM1501 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1501 RNA, herein designated VGAM RNA, and which when bound by VGAM1501 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1501 host target proteins.

[20978] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1501 gene, herein designated VGAM GENE, on one or more VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20979] It is yet further appreciated that a function of VGAM1501 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1501 include diagnosis, prevention and treatment of viral infection by Rat cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1501 correlate with, and may be deduced from, the identity of the host target genes which VGAM1501 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[20980] Nucleotide sequences of the VGAM1501 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1501 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1501 are further described hereinbelow with reference to Table 1.

[20981] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1501 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20982] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1502 (VGAM1502) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20983] VGAM1502 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1502 was detected is described hereinabove with reference to Figs. 2–8.

[20984] VGAM1502 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus. VGAM1502 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20985] VGAM1502 gene, herein designated VGAM GENE, encodes a VGAM1502 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1502 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1502 precursor RNA is designated SEQ ID:37749, and is provided hereinbelow with reference to the sequence listing part.

[20986] VGAM1502 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1502 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the



fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[20987] An enzyme complex designated DICER COMPLEX, dices the VGAM1502 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1502 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1502 RNA is designated SEQ ID:37750, and is provided hereinbelow with reference to the sequence listing part.

[20988] VGAM1502 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and

a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[20989] VGAM1502 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1502 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both

3UTR and 5UTR regions.

[20990] The complementary binding of VGAM1502 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1502 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[20991] It is appreciated that VGAM1502 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1502 host target genes. The mRNA of each one of this plurality of VGAM1502 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1502 RNA, herein designated VGAM RNA, and which when bound by VGAM1502 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1502 host target proteins.

[20992] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1502 gene, herein designated VGAM GENE, on one or more VGAM1502 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[20993] It is yet further appreciated that a function of VGAM1502 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1502 correlate with, and may be deduced from, the identity of the host target genes which VGAM1502 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[20994] Nucleotide sequences of the VGAM1502 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1502 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1502 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1502 are further described hereinbelow with reference to Table 1.

[20995] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1502 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[20996] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1503 (VGAM1503) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[20997] VGAM1503 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1503 was detected is described hereinabove with reference to Figs. 2–8.

[20998] VGAM1503 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[20999] VGAM1503 gene, herein designated VGAM GENE, encodes a VGAM1503 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1503 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1503 precursor RNA is designated SEQ ID:37759, and is provided hereinbelow with reference to the sequence listing part.

[21000] VGAM1503 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the

RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21001] An enzyme complex designated DICER COMPLEX, dices the VGAM1503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1503 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1503 RNA is designated SEQ ID:37760, and is provided hereinbelow with reference to the sequence listing part.

[21002] VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN COD-

ING and 3UTR respectively.

[21003] VGAM1503 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1503 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.



[21004] The complementary binding of VGAM1503 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1503 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21005] It is appreciated that VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1503 host target genes. The mRNA of each one of this plurality of VGAM1503 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1503 RNA, herein designated VGAM RNA, and which when bound by VGAM1503 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1503 host target proteins.

[21006] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1503 gene, herein designated VGAM GENE, on one

or more VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21007] It is yet further appreciated that a function of VGAM1503 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1503 correlate with, and may be deduced from, the identity of the host target genes which VGAM1503 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21008] Nucleotide sequences of the VGAM1503 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1503 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1503 are further described hereinbelow with reference to Table 1.

[21009] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1503 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21010] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1504 (VGAM1504) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21011] VGAM1504 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1504 was detected is de-

scribed hereinabove with reference to Figs. 2–8.

[21012] VGAM1504 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia herpesvirus.

VGAM1504 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21013] VGAM1504 gene, herein designated VGAM GENE, encodes a VGAM1504 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1504 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1504 precursor RNA is designated SEQ ID:37766, and is provided hereinbelow with reference to the sequence listing part.

[21014] VGAM1504 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1504 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial

inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21015] An enzyme complex designated DICER COMPLEX, dices the VGAM1504 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1504 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1504 RNA is designated SEQ ID:37767, and is provided hereinbelow with reference to the sequence listing part.

[21016] VGAM1504 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21017] VGAM1504 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1504 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1504 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21018] The complementary binding of VGAM1504 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1504 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21019] It is appreciated that VGAM1504 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1504 host target genes. The mRNA of each one of this plurality of VGAM1504 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1504 RNA, herein designated VGAM RNA, and which when bound by VGAM1504 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1504 host target proteins.

[21020] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1504 gene, herein designated VGAM GENE, on one or more VGAM1504 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21021] It is yet further appreciated that a function of VGAM1504 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1504 include diagnosis, prevention and treatment of viral infection by Tupaia herpesvirus. Specific functions, and accordingly utilities, of VGAM1504 correlate with, and may be deduced from, the identity of the host target genes which VGAM1504 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21022] Nucleotide sequences of the VGAM1504 precursor RNA,



herein designated VGAM PRECURSOR RNA, and of the diced VGAM1504 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1504 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1504 are further described hereinbelow with reference to Table 1.

[21023] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1504 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21024] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1505 (VGAM1505) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21025] VGAM1505 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1505 was detected is described hereinabove with reference to Figs. 2-8.

[21026] VGAM1505 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ateline herpesvirus 3. VGAM1505 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21027] VGAM1505 gene, herein designated VGAM GENE, encodes a VGAM1505 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1505 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1505 precursor RNA is designated SEQ ID:37772, and is provided hereinbelow with reference to the sequence listing part.

[21028] VGAM1505 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1505 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of

the second half thereof.

[21029] An enzyme complex designated DICER COMPLEX, dices the VGAM1505 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1505 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1505 RNA is designated SEQ ID:37773, and is provided hereinbelow with reference to the sequence listing part.

[21030] VGAM1505 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21031] VGAM1505 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1505 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21032] The complementary binding of VGAM1505 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1505 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21033] It is appreciated that VGAM1505 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1505 host target genes. The mRNA of each one of this plurality of VGAM1505 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1505 RNA, herein designated VGAM RNA, and which when bound by VGAM1505 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1505 host target proteins.

[21034] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1505 gene, herein designated VGAM GENE, on one or more VGAM1505 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21035] It is yet further appreciated that a function of VGAM1505 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of viral infection by Ateline herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1505 correlate with, and may be deduced from, the identity of the host target genes which VGAM1505 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21036] Nucleotide sequences of the VGAM1505 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

diced VGAM1505 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1505 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1505 are further described hereinbelow with reference to Table 1.

[21037] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1505 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21038] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1506 (VGAM1506) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21039] VGAM1506 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1506 was detected is described hereinabove with reference to Figs. 2-8.

[21040] VGAM1506 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21041] VGAM1506 gene, herein designated VGAM GENE, encodes a VGAM1506 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1506 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1506 precursor RNA is designated SEQ ID:37798, and is provided hereinbelow with reference to the sequence listing part.

[21042] VGAM1506 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.



[21043] An enzyme complex designated DICER COMPLEX, dices the VGAM1506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1506 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1506 RNA is designated SEQ ID:37799, and is provided hereinbelow with reference to the sequence listing part.

[21044] VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21045] VGAM1506 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1506 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1506 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21046] The complementary binding of VGAM1506 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1506 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1506 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1506 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21047] It is appreciated that VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1506 host target genes. The mRNA of each one of this plurality of VGAM1506 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1506 RNA, herein designated VGAM RNA, and which when bound by VGAM1506 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1506 host target proteins.

[21048] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1506 gene, herein designated VGAM GENE, on one or more VGAM1506 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21049] It is yet further appreciated that a function of VGAM1506 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1506 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1506 correlate with, and may be deduced from, the identity of the host target genes which VGAM1506 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21050] Nucleotide sequences of the VGAM1506 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1506 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM1506 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1506 are further described hereinbelow with reference to Table 1.

[21051] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1506 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21052] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1507 (VGAM1507) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21053] VGAM1507 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1507 was detected is described hereinabove with reference to Figs. 2-8.

[21054] VGAM1507 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Amsacta moorei* ento-

mopoxvirus. VGAM1507 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21055] VGAM1507 gene, herein designated VGAM GENE, encodes a VGAM1507 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1507 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1507 precursor RNA is designated SEQ ID:37803, and is provided hereinbelow with reference to the sequence listing part.

[21056] VGAM1507 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1507 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21057] An enzyme complex designated DICER COMPLEX, dices

the VGAM1507 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1507 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1507 RNA is designated SEQ ID:37804, and is provided hereinbelow with reference to the sequence listing part.

[21058] VGAM1507 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21059] VGAM1507 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1507 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1507 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1507 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21060] The complementary binding of VGAM1507 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE



II and BINDING SITE III, inhibits translation of VGAM1507 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1507 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21061] It is appreciated that VGAM1507 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1507 host target genes. The mRNA of each one of this plurality of VGAM1507 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1507 RNA, herein designated VGAM RNA, and which when bound by VGAM1507 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1507 host target proteins.

[21062] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1507 gene, herein designated VGAM GENE, on one or more VGAM1507 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21063] It is yet further appreciated that a function of VGAM1507 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1507 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1507 correlate with, and may be deduced from, the identity of the host target genes which VGAM1507 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21064] Nucleotide sequences of the VGAM1507 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1507 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM1507 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1507 are further described hereinbelow with reference to Table 1.

[21065] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1507 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21066] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1508 (VGAM1508) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21067] VGAM1508 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1508 was detected is described hereinabove with reference to Figs. 2-8.

[21068] VGAM1508 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM1508 host target gene, herein design-

nated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21069] VGAM1508 gene, herein designated VGAM GENE, encodes a VGAM1508 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1508 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1508 precursor RNA is designated SEQ ID:37806, and is provided hereinbelow with reference to the sequence listing part.

[21070] VGAM1508 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1508 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21071] An enzyme complex designated DICER COMPLEX, dices the VGAM1508 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, into VGAM1508 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1508 RNA is designated SEQ ID:37807, and is provided hereinbelow with reference to the sequence listing part.

[21072] VGAM1508 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21073] VGAM1508 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1508 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1508 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21074] The complementary binding of VGAM1508 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1508 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1508

host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1508 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21075] It is appreciated that VGAM1508 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1508 host target genes. The mRNA of each one of this plurality of VGAM1508 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1508 RNA, herein designated VGAM RNA, and which when bound by VGAM1508 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1508 host target proteins.

[21076] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1508 gene, herein designated VGAM GENE, on one or more VGAM1508 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21077] It is yet further appreciated that a function of VGAM1508 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1508 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1508 correlate with, and may be deduced from, the identity of the host target genes which VGAM1508 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21078] Nucleotide sequences of the VGAM1508 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1508 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1508 folded precursor RNA, herein designated



VGAM FOLDED PRECURSOR RNA, of VGAM1508 are further described hereinbelow with reference to Table 1.

[21079] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1508 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21080] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1509 (VGAM1509) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21081] VGAM1509 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1509 was detected is described hereinabove with reference to Figs. 2-8.

[21082] VGAM1509 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[21083] VGAM1509 gene, herein designated VGAM GENE, encodes a VGAM1509 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1509 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1509 precursor RNA is designated SEQ ID:37810, and is provided hereinbelow with reference to the sequence listing part.

[21084] VGAM1509 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21085] An enzyme complex designated DICER COMPLEX, dices the VGAM1509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1509 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1509 RNA is designated SEQ ID:37811, and is provided hereinbelow with reference to the sequence listing part.

[21086] VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21087] VGAM1509 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1509 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1509 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21088] The complementary binding of VGAM1509 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1509 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1509 host target RNA, herein designated VGAM HOST TARGET

RNA, into VGAM1509 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21089] It is appreciated that VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1509 host target genes. The mRNA of each one of this plurality of VGAM1509 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1509 RNA, herein designated VGAM RNA, and which when bound by VGAM1509 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1509 host target proteins.

[21090] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1509 gene, herein designated VGAM GENE, on one or more VGAM1509 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21091] It is yet further appreciated that a function of VGAM1509 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1509 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1509 correlate with, and may be deduced from, the identity of the host target genes which VGAM1509 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21092] Nucleotide sequences of the VGAM1509 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the dived VGAM1509 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1509 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1509 are further

described hereinbelow with reference to Table 1.

[21093] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1509 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21094] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1510 (VGAM1510) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21095] VGAM1510 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1510 was detected is described hereinabove with reference to Figs. 2-8.

[21096] VGAM1510 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21097] VGAM1510 gene, herein designated VGAM GENE, encodes a VGAM1510 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1510 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1510 precursor RNA is designated SEQ ID:37819, and is provided hereinbelow with reference to the sequence listing part.

[21098] VGAM1510 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21099] An enzyme complex designated DICER COMPLEX, dices the VGAM1510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1510 RNA, herein designated VGAM RNA, a single stranded ~22 nt



long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1510 RNA is designated SEQ ID:37820, and is provided hereinbelow with reference to the sequence listing part.

[21100] VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21101] VGAM1510 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1510 RNA, herein designated

VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1510 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21102] The complementary binding of VGAM1510 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1510 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1510 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21103] It is appreciated that VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1510 host target genes. The mRNA of each one of this plurality of VGAM1510 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1510 RNA, herein designated VGAM RNA, and which when bound by VGAM1510 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1510 host target proteins.

[21104] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1510 gene, herein designated VGAM GENE, on one or more VGAM1510 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21105] It is yet further appreciated that a function of VGAM1510 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1510 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1510 correlate with, and may be deduced from, the identity of the host target genes which VGAM1510 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21106] Nucleotide sequences of the VGAM1510 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1510 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1510 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1510 are further described hereinbelow with reference to Table 1.

[21107] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1510 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21108] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1511 (VGAM1511) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21109] VGAM1511 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1511 was detected is described hereinabove with reference to Figs. 2-8.

[21110] VGAM1511 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21111] VGAM1511 gene, herein designated VGAM GENE, encodes

a VGAM1511 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1511 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1511 precursor RNA is designated SEQ ID:37823, and is provided hereinbelow with reference to the sequence listing part.

[21112] VGAM1511 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21113] An enzyme complex designated DICER COMPLEX, dices the VGAM1511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1511 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1511 RNA is designated SEQ ID:37824, and is provided hereinbelow with reference to the sequence listing part.

[21114] VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21115] VGAM1511 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1511 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed

sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1511 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21116] The complementary binding of VGAM1511 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1511 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1511 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target



protein is therefore outlined by a broken line.

[21117] It is appreciated that VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1511 host target genes. The mRNA of each one of this plurality of VGAM1511 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1511 RNA, herein designated VGAM RNA, and which when bound by VGAM1511 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1511 host target proteins.

[21118] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1511 gene, herein designated VGAM GENE, on one or more VGAM1511 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21119] It is yet further appreciated that a function of VGAM1511 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1511 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1511 correlate with, and may be deduced from, the identity of the host target genes which VGAM1511 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21120] Nucleotide sequences of the VGAM1511 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1511 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1511 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1511 are further described hereinbelow with reference to Table 1.

[21121] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1511 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21122] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1512 (VGAM1512) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21123] VGAM1512 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1512 was detected is described hereinabove with reference to Figs. 2-8.

[21124] VGAM1512 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox virus.

VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21125] VGAM1512 gene, herein designated VGAM GENE, encodes a VGAM1512 precursor RNA, herein designated VGAM

PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1512 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1512 precursor RNA is designated SEQ ID:37831, and is provided hereinbelow with reference to the sequence listing part.

[21126] VGAM1512 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21127] An enzyme complex designated DICER COMPLEX, dices the VGAM1512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1512 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1512 RNA is designated SEQ ID:37832, and is provided hereinbelow with reference to the sequence listing part.

[21128] VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21129] VGAM1512 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1512 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host

target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1512 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21130] The complementary binding of VGAM1512 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1512 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1512 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21131] It is appreciated that VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1512 host target genes. The mRNA of each one of this plurality of VGAM1512 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1512 RNA, herein designated VGAM RNA, and which when bound by VGAM1512 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1512 host target proteins.

[21132] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1512 gene, herein designated VGAM GENE, on one or more VGAM1512 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21133] It is yet further appreciated that a function of VGAM1512 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1512 include diagnosis, prevention and treatment of viral infection by Fowlpox virus. Specific functions, and accordingly utilities, of VGAM1512 correlate with, and may be deduced from, the identity of the host target genes which VGAM1512 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21134] Nucleotide sequences of the VGAM1512 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1512 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1512 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1512 are further described hereinbelow with reference to Table 1.

[21135] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of



Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1512 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21136] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1513 (VGAM1513) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21137] VGAM1513 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1513 was detected is described hereinabove with reference to Figs. 2-8.

[21138] VGAM1513 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta moorei entomopoxvirus. VGAM1513 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21139] VGAM1513 gene, herein designated VGAM GENE, encodes a VGAM1513 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and un-

like most ordinary genes, VGAM1513 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1513 precursor RNA is designated SEQ ID:37834, and is provided hereinbelow with reference to the sequence listing part.

[21140] VGAM1513 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1513 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21141] An enzyme complex designated DICER COMPLEX, dices the VGAM1513 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1513 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide sequence of VGAM1513 RNA is designated SEQ ID:37835, and is provided hereinbelow with reference to the sequence listing part.

[21142] VGAM1513 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21143] VGAM1513 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1513 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3

such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1513 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21144] The complementary binding of VGAM1513 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1513 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1513 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21145] It is appreciated that VGAM1513 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1513 host target genes. The mRNA of each one of this plurality of VGAM1513 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1513 RNA, herein designated VGAM RNA, and which when bound by VGAM1513 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1513 host target proteins.

[21146] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1513 gene, herein designated VGAM GENE, on one or more VGAM1513 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).

[21147] It is yet further appreciated that a function of VGAM1513 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1513 include diagnosis, prevention and treatment of viral infection by Amsacta moorei entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1513 correlate with, and may be deduced from, the identity of the host target genes which VGAM1513 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21148] Nucleotide sequences of the VGAM1513 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1513 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1513 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1513 are further described hereinbelow with reference to Table 1.

[21149] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the

complementarity of each of these host target binding sites to VGAM1513 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21150] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1514 (VGAM1514) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21151] VGAM1514 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1514 was detected is described hereinabove with reference to Figs. 2–8.

[21152] VGAM1514 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turnip crinkle virus. VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21153] VGAM1514 gene, herein designated VGAM GENE, encodes a VGAM1514 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1514 precursor RNA,

herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1514 precursor RNA is designated SEQ ID:37849, and is provided hereinbelow with reference to the sequence listing part.

[21154] VGAM1514 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21155] An enzyme complex designated DICER COMPLEX, dices the VGAM1514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1514 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other



necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1514 RNA is designated SEQ ID:37850, and is provided hereinbelow with reference to the sequence listing part.

[21156] VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21157] VGAM1514 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1514 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I,

BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1514 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21158] The complementary binding of VGAM1514 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1514 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1514 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21159] It is appreciated that VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1514 host target genes. The mRNA of each one of this plurality of VGAM1514 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1514 RNA, herein designated VGAM RNA, and which when bound by VGAM1514 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1514 host target proteins.

[21160] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1514 gene, herein designated VGAM GENE, on one or more VGAM1514 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

Perspective: Glimpses of a tiny RNA world, Science  
294,779 (2001)).

- [21161] It is yet further appreciated that a function of VGAM1514 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1514 include diagnosis, prevention and treatment of viral infection by Turnip crinkle virus. Specific functions, and accordingly utilities, of VGAM1514 correlate with, and may be deduced from, the identity of the host target genes which VGAM1514 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.
- [21162] Nucleotide sequences of the VGAM1514 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1514 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1514 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1514 are further described hereinbelow with reference to Table 1.
- [21163] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites

to VGAM1514 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[21164] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1515 (VGAM1515) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21165] VGAM1515 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1515 was detected is described hereinabove with reference to Figs. 2-8.

[21166] VGAM1515 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine foamy virus. VGAM1515 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21167] VGAM1515 gene, herein designated VGAM GENE, encodes a VGAM1515 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1515 precursor RNA, herein designated VGAM PRECURSOR RNA, does not en-

code a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1515 precursor RNA is designated SEQ ID:37886, and is provided hereinbelow with reference to the sequence listing part.

[21168] VGAM1515 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21169] An enzyme complex designated DICER COMPLEX, dices the VGAM1515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1515 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 35%) nucleotide se-

quence of VGAM1515 RNA is designated SEQ ID:37887, and is provided hereinbelow with reference to the sequence listing part.

[21170] VGAM1515 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21171] VGAM1515 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1515 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is ap-

preciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1515 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21172] The complementary binding of VGAM1515 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1515 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1515 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21173] It is appreciated that VGAM1515 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1515 host target genes. The mRNA of



each one of this plurality of VGAM1515 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1515 RNA, herein designated VGAM RNA, and which when bound by VGAM1515 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1515 host target proteins.

[21174] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1515 gene, herein designated VGAM GENE, on one or more VGAM1515 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science

294,779 (2001)).

[21175] It is yet further appreciated that a function of VGAM1515 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1515 include diagnosis, prevention and treatment of viral infection by Equine foamy virus. Specific functions, and accordingly utilities, of VGAM1515 correlate with, and may be deduced from, the identity of the host target genes which VGAM1515 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[21176] Nucleotide sequences of the VGAM1515 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the diced VGAM1515 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1515 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1515 are further described hereinbelow with reference to Table 1.

[21177] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on, and schematic representation of the complementarity of each of these host target binding sites to VGAM1515 RNA, herein designated VGAM RNA, are de-

scribed hereinbelow with reference to Table 2.

[21178] Fig. 1 further provides a conceptual description of another novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1516 (VGAM1516) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[21179] VGAM1516 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1516 was detected is described hereinabove with reference to Figs. 2–8.

[21180] VGAM1516 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human foamy virus. VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[21181] VGAM1516 gene, herein designated VGAM GENE, encodes a VGAM1516 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1516 precursor RNA, herein designated VGAM PRECURSOR RNA, does not encode a protein. A nucleotide sequence identical or highly

similar to the nucleotide sequence of VGAM1516 precursor RNA is designated SEQ ID:37904, and is provided hereinbelow with reference to the sequence listing part.

[21182] VGAM1516 precursor RNA, herein designated VGAM PRECURSOR RNA, folds onto itself, forming VGAM1516 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional hairpin structure. As is well known in the art, this hairpin structure, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[21183] An enzyme complex designated DICER COMPLEX, dices the VGAM1516 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, into VGAM1516 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, dicing of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 28%) nucleotide sequence of VGAM1516 RNA is designated SEQ ID:37905,

and is provided hereinbelow with reference to the sequence listing part.

[21184] VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA, comprises three regions, as is typical of mRNA of a protein coding gene: a 5 untranslated region, a protein coding region and a 3 untranslated region, designated 5UTR, PROTEIN CODING and 3UTR respectively.

[21185] VGAM1516 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1516 RNA, herein designated VGAM RNA, is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites

shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting VGAM1516 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3UTR region, this is meant as an example only these host target binding sites may be located in the 3UTR region, the 5UTR region, or in both 3UTR and 5UTR regions.

[21186] The complementary binding of VGAM1516 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1516 host target RNA, herein designated VGAM HOST TARGET RNA, into VGAM1516 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[21187] It is appreciated that VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1516 host target genes. The mRNA of each one of this plurality of VGAM1516 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1516 RNA, herein designated VGAM RNA, and which when bound by VGAM1516 RNA, herein designated VGAM RNA, causes inhibition of translation of respective one or more VGAM1516 host target proteins.

[21188] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1516 gene, herein designated VGAM GENE, on one or more VGAM1516 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., Perspective: Glimpses of a tiny RNA world, Science 294,779 (2001)).